EXPLOSION and Blast-Related Injuries

Effects of Explosion and Blast from Military Operations and Acts of Terrorism

Edited by Nabil M. ELSAYED James L. ATKINS

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Editors

Nabil M. Elsayed
Department of Early Drug Development
Celgene Corp.
Summit, NJ
and
Department of Anatomy and Cell Biology
SUNY Medical Center
Brooklyn, NY

James L. Atkins
Division of Military Casualty Research
Walter Reed Army Institute of Research
Silver Spring, MD

Associate Editor

Nikolai V. Gorbunov
Department of Scientific Research
Armed Forces Radiobiology Research Institute
Bethesda, MD

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List of Contributors

Aharonson-Daniel, Limor, PhD. Israel National Center for Trauma and Emergency Medicine, Gertner Institute for Epidemiology and Health Policy Research, Sheba Medical Center, Israel

Alisov, Petr G., MD. Department of Surgery, City Clinic, St. Petersburg, Russian Federation

Almogy, Gidon, MD. Department of General Surgery, Hadassah University Hospital, Jerusalem, Israel

Armonda, Rocco, MD. Department of Neurosurgery, Walter Reed Army Medical Center, Washington, DC, USA

Asher, Ludmila V., MD. Division of Pathology. Walter Reed Army Institute of Research, Silver Spring, MD, USA

Atkins, James L., MD, PhD. Division of Military Casualty Research, Division of Pathology. Walter Reed Army Institute of Research, Silver Spring, MD, USA

Bahouth, Hany, MD. Surgery B Department and Trauma Unit, Rambam Health Campus, Haifa, Israel

Bandak, Faris, PhD. Department of Neurology, F. Edward Hébert School of Medicine, Uniformed Services, University of the Health Sciences, Bethesda, MD, USA

Blackbourne, Lorne H., MD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Branica, Srećko, MD, PhD. Department of Otorhinolaryngology, University Hospital Center, Zagreb, Croatia

Coronado, Victor G., MD, MPH. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA, USA

Dawidowsky, Krsto, MD, MS. Department of Otorhinolaryngology, University Hospital Center, Zagreb, Croatia

Dubick, Michael, PhD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Eastridge, Brian J., MD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Ecklund, James, MD. Dept. of Neurosurgery, Walter Reed Army Medical Center, Washington, DC, USA

Elsayed, Nabil M. PhD., FATS. Department of Early Drug Development, Celgene Corp., Summit, NJ, and Department of Anatomy, and Cell Biology, SUNY, Medical Center, Brooklyn, NY, USA

Feigenberg, Zvi, MD. Medical Division, Magen David Adom, Israel

Gorbunov, Nikolai V., PD. Department of Scientific Research, Armed Forces Radiobiology Institute, Bethesda, MD, USA

Grant, Gerald, MD. Department of Neurosurgery, Duke University Medical Center, Durham, NC, USA

Holcomb, John B., MD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Kauvar, David S., MD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Kirkman, Emrys, PhD. Biophysics and Trauma (Surgical Science), Biomedical Sciences, Defence Science and Technology Laboratory (Dstl), Porton Down, Salisbury, UK

Kluger, Yoram, MD, FACS. Rappaport School of Medicine, Technion, Technological Institute of Israel and Division of General Surgery B, Rambam Medical Center, Haifa, Israel

Ling, Geoffrey, MD, PhD. Department of Neurology, F. Edward Hébert School of Medicine, Uniformed Services, University of the Health Sciences, Bethesda, MD, and Department of Critical Care Medicine, Neurology and Neurosurgery, Walter Reed Army Medical Center, Washington, DC, USA

McKinnon, Brian J., MD. Department of Otolaryngology—Head and Neck Surgery, Medical College of Georgia, Augusta, GA, USA

Peleg, Kobi, PhD, MPH. Israel National Center for Trauma and Emergency Medicine, Gertner Institute for Epidemiology and Health Policy Research, Sheba Medical Center, and The Multidisciplinary Program for Emergency and Disaster Management, School of Public Health, Tel-Aviv University, Tel-Aviv, Israel

Przekwas, Andrzej, PhD. Computational Medicine and Biology Division, CFD Research Corp., Huntsville, AL, USA

Ritenour, Amber E., MD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Rivkind, Avraham I., MD. General Surgery and Shock Trauma Unit, Hadassah University, Hospital, Jerusalem, Israel

Sapsford, Wayne, MD. FRCS. Royal Air Force, UK

Sasser, Scott M., MD. Department of Emergency Medicine, Emory University School of Medicine, Atlanta, GA, USA

Sattin, Richard W., MD. Department of Emergency Medicine, Medical College of Georgia, Augusta, GA, USA

Sawdon, Marina, PhD. School for Health, University of Durham, UK.

Šprem, Nikola, MD, PhD. Department of Otorhinolaryngology, University Hospital Center, Zagreb, Croatia

Sullivent III, Ernest E., MD. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA, USA

Tadmor, Boaz, MD. Tel Aviv University Faculty of Medicine, School of Public Health: The Multidisciplinary Program for Emergency and Disaster Management, Tel-Aviv, Israel

Tsokos, Michael, MD. Institute of Legal Medicine and Forensic Sciences, Berlin, Germany

Wade, Charles E., PhD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Watts, Sarah, PhD. MRCVS, Biophysics and Trauma (Surgical Science), Biomedical Sciences, Dstl Porton Down, Salisbury, UK

Wolf, Steven E., MD. U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, USA

Young, Lee Ann. MS Applied Research Associates, Inc., San Antonio, TX, USA

Preface

With almost daily news reports of explosions somewhere in the world, we are constantly reminded that explosion-related injuries can occur unexpectedly in both military and civilian populations. Because of the increased incidence of explosion-induced injuries, many physicians have first-hand experience with treating blast-injured casualties, and their insights, gained at a dear price, have led to improvements in care. The experience is worldwide and a consolidation of lessons learned would be invaluable.

This book is a first step in that direction and arguably the most extensive review since *Textbook of Military Medicine* was first published in 1991.

Understanding of explosion injury also has benefited over the years from the parallel extensive research conducted in the laboratory by dedicated scientists, engineers, and computer programmers to advance our knowledge of the mechanisms of injury, and to develop more efficient mass casualty and disaster management paradigms. This book provides an overview of some important areas of this research.

There is clear diversity in the experience of some of the authors, emphasizing that the characteristics of explosions can vary widely either by circumstance or by intent, and the resulting injuries also may vary. Moreover the book brings together a variety of experiences from different parts of the world where the authors have dealt with specific injury patterns. Early recognition of the injury pattern may be important in orchestrating the most effective mass casualty response. Despite this progress there is still much to learn about explosion-related injuries, and further research in this area is urgently needed. As discussed in the first chapter of this book there are still questions about terminology and classification systems, and this will be evident to the reader in subtle differences in the definitions of primary, secondary, tertiary, and quaternary injuries, and in the classification of combined injuries used by various authors.

This book summarizes some of the progress in understanding the pathophysiological consequences of blast-induced injuries and suggests future

research directions. The review is not all-inclusive, and some information about the physics of explosions or the construction of explosive devices has been excluded intentionally.

Explosion and Blast-Related Injuries provides an overview of the field, which is suitable as a starting point for researchers interested in studying casualty response systems or the mechanisms of blast-induced injuries. It is important to note that it is not a manual for medical care of blast-injured casualties. We hope that this book will be helpful to physicians receiving blast-injured casualties by providing a broader perspective that might help them recognize new injury patterns resulting from a change in threat, and to scientists and engineers that consider joining the field of explosion and blast-injury research.

The field is expansive and the book is divided into four parts: Part 1—Epidemiology of Blast and Explosion Injury; Part 2—Pathology and Pathophysiology of Blast Injuries; Part 3—Modeling and Mechanisms of Primary Blast Injury; and Part 4—Global Experiences of Blast Injury and Mass Casualty Management.

The editors wish to thank Drs. Robert Vandre and Kenneth Bertram for their continuous support and encouragement, and Dr. Debra Yourick for her assistance in reviewing the manuscript.

Introduction

The United States Department of Defense has recognized the potential occupational health hazards associated with explosive devices on the battlefield. Such devices are designed to be lethal, but when deployed against an adversary, they must also be safe to use. Explosive weaponry often employs systems that generate dangerously high decibel and blast overpressure levels capable of causing permanent injury to the unprotected user of such weapons. Therefore, the U.S. military, over the many years, has implemented occupational health programs with such weapons systems to eliminate or mitigate health risks to the warfighter, while developing protective measures against blast on the battlefield.

Recent experiences in Iraq and Afghanistan have brought into focus the need for improved soldier-based protective systems and other interventions to protect the warfighter against improvised explosive devices (IEDs). The employment of powerful IEDs by terrorists also has necessitated the need to understand the nature of injuries caused by such devices. This need for understanding includes appreciating the multisystem effects of blast on different organs and tissues of the body. The wounds from explosive devices are complex, and the management and care will depend on the type and severity of injuries.

With the increased incidence of global terrorism against nonmilitary targets, new attention has been directed toward injuries in civilian populations. Therefore, concerted efforts at understanding the pathophysiology of blast injury, risk factors, types of injury, and methods to promote recovery from such injuries are of paramount importance. It also is recognized that unlike military populations, civilians would have little personal physical protection at the time of a terrorist explosion. Well-defined policies that extend across basic and applied research, product development, epidemiology, and surveillance and medical care are necessary and must be updated based on new capabilities and evolving threats.

This book will address only a few aspects of such injuries, and the impact of high intensity blast, mines, penetrating shrapnel, and burn on the human body both actual and computer-simulated. It is not intended to be all-inclusive, but to discuss areas that deserve immediate attention through research and policy.

It is often difficult to differentiate a situational psychological response from actual neurological damage. Understandably, the psychological effect associated with a sudden disorienting explosion, with accompanying hearing loss, difficulty in breathing, or nonspecific pain can be psychologically stressful. Differentiating psychological effects from those related to actual physical injury is one of the continuing challenges in medical management.

The resulting injuries sustained from a detonation of an explosive device vary, depending on the type of explosive(s), the manner in which the device is employed, the physical environment that may determine the degree and type of injuries, and the susceptibility of the targeted population to injury. It is generally recognized that blast injuries that result in rupturing of the tympanic membranes follow sudden pressure increases up to at least 6 psi at levels of at least 160 decibels (sound) or 185 decibels (nonperiodic pressure). With lung injury resulting in rupture, it can be assumed that levels of 200 decibels (15 psi) were reached and the risk of lung emboli is high. However, in many instances, the absence of damage to the tympanic membranes could still be associated with dangerously high decibel exposure and cannot be used as a measure of actual exposure. This only adds to the confusion in determining actual exposure.

With the sudden expansion and compression of air generating positive overpressure and negative underpressure waves, the hollow organs of the body, including the ears, lungs, sinuses, and organs in the abdominal cavity, such as the bowels, are highly susceptible to rupture. It is now recognized that explosions can also cause direct injury to the brain, possibly disrupting neural pathways with resulting long-term deficits and conceivably predisposing individuals to neurodegeneration. This is one of the current concerns associated with traumatic brain injury (TBI) in injured soldiers returning from the Middle East.

Despite our outstanding medical delivery systems, the assessment of acute injury from blast is still poorly understood. No reliable prognosticators of

blast injury exist, nor are there predictors of susceptibility to injury. The initial medical consequences often overshadow concerns for the long-term health effects, so injured individuals who recover are often lost to follow-up. The impact of sudden changes in atmospheric pressure on highly sensitive organs, to include the brain, is also poorly understood, and pragmatic ways to address serious lung injury need to be defined to reduce mortality. In addition, the impact of blast on an infant or child who has not yet physically matured is unknown. Such questions can be answered only through longitudinal studies and basic and applied research using appropriate animal models.

It has become increasingly evident that terrorism is a multifaceted threat. Terrorists have access to explosives of all kinds, improvised delivery systems, and projectiles that make the explosive threat even more lethal. The possibility of using blast and heat with chemical, biological, and radiological agents to inflict "combined injuries" represents a greater therapeutic challenge with its potential impact even on the immune system.

It is hoped that this book will generate interest in this very important topic of blast injury. The implications extend to both our military and civilian communities.

Ernest T. Takafuji, MD, MPH
Colonel, U.S. Army (Retired),
Former Commander,
Walter Reed Army Institute of Research,
Washington, DC

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PART 1

Epidemiology of Blast and Explosion Injuries

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CHAPTER 1

The Epidemiology and Triage of Blast Injuries

Richard W. Sattin, Scott M. Sasser,
Ernest E. Sullivent III, and Victor G. Coronado

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INTRODUCTION

Injuries from explosive materials due to terrorism or other causes are a constant threat that happen worldwide, and they present unique triage, diagnostic, and management challenges. Although these casualty events often occur indiscriminately, the type and pattern of injuries to victims are predictable. Moreover, the number of victims can quickly overwhelm the capacity of the health care system. In the United States, preparedness for mass casualty events, however, has focused primarily on the threat of biological, chemical, radiation, and nuclear weapons. As recent events in New York City, Madrid, London, and Mumbai have shown, terrorism using conventional weapons and explosive devices is a far more likely scenario, and these events highlight the terrorists' increasing coordination, complexity, and capacity to inflict injury and death. In fact, explosions occur almost daily somewhere in the world. The recent past has seen a change in terrorism, both ideologically, with an evolution from predominantly nationalist movements, to multinational, global organizations (United States Government [US] 2003) and operationally, with the utilization of different tactics and technology, and a resultant increasing lethality to their bombings (Lesser et al. 1999; United States General Accounting Office [GAO] 2003a; Mayo & Kluger 2006). Other than physicians who have served in trauma settings in Iraq or Afghanistan, few physicians in the United States either have been trained in the care of the injured blast victim or have taken care of a patient who has sustained injuries from an explosion. Therefore, the care for those injured from explosive devices remains a real and ongoing concern for acute injury care providers. Moreover, if a large explosion-related mass casualty event occurs on an already fragile and overburdened response system, the results will likely be less than optimal for victims. Understanding the epidemiology of explosion-related events from nations that have experienced conventional weapon attacks on their civilian population is critical to improving preparedness in the United States and worldwide.

To understand the concepts of injuries from explosions, one must also understand the concepts of injury control. As with other diseases, injuries can be viewed as a problem in medical ecology—that is, as a relationship between a person (the host), an agent, and the environment (Haddon 1970; Haddon & Baker 1981; Sattin 1992). Unlike other diseases, the underlying agent of injury is not a microbe or carcinogen, but energy, most

often in the form of mechanical force (Haddon 1970). The dose of energy received, the dose's distribution, duration, and rapidity, and the individual's response to the transfer of the energy can determine if a physical injury occurs or is prevented (Committee on Trauma Research 1985). For example, a large mechanical energy load quickly transmitted to a hip during a fall involving an older person may lead to a fracture. If that same energy load could be dissipated through use of energy-absorbing flooring or mats or through hip pads or other new technologies, fewer persons would sustain hip fractures. Similarly, the percentage of deaths due to thoracic and traumatic brain injuries is significantly reduced through the use of body armor in military personnel (Lew 2005).

The basic injury paradigm of host, agent, and environment also needs to include the effect of the social environment. Victims of explosions can experience factors other than physical injury such as adverse mental health consequences including depression, anxiety, and low self-esteem, and harmful physical health consequences such as suicide attempts, cardiovascular disease, and substance abuse (National Center for Injury Prevention and Control [NCIPC] 2002). Any of these consequences can lead to hospitalization, disability, or death. The emotional, financial, and psychosocial effects of an acute injury may be even more debilitating than the actual physical injury. The severity of these effects is an essential determinant of long-term functionality. An acute injury has not just an immediate effect on the injured person, but also a long-term "ripple effect" on that person's life and the lives of others in his or her family and community. For example, an injured father may face temporary or permanent loss of income, changes in the relationship with his wife, and an inability to care for his children. His wife may shift from spouse to caregiver and may take on responsibility for the family's income. His children may experience emotional trauma not only from their father's injury but from changes in their routine or living situation. Health care providers are also subject to psychosocial problems resulting from caring for the acutely injured and their families. In the case of a mass casualty or disaster event, these ripple effects may affect a community's societal and functional infrastructure extensively.

Injury leads to pathological conditions and impaired physiological functioning that can affect any part, organ, or system of an individual and can have both short-term and long-term effects (Sattin 1992). Due to the potential extensive nature of the disease, outcomes are dependent on a

broad continuum of multidisciplinary care. Injury has been described, until recently, as the "neglected disease" since it occurs in such great numbers, but has been tacitly accepted as a normal occurrence of living in a modern society (Committee on Trauma, and Committee on Shock, Division of Medical Sciences, National Academy of Sciences/National Research Council 1966). However, the 1985 report, *Injury in America*, noted that a public health approach similar to that used for other diseases could lead to significant reduction in injuries (Committee on Trauma Research, Commission on Life Sciences, National Research Council and the Institute of Medicine 1985).

The classification of injury poses a number of epidemiological issues. We can classify injuries by the actual nature of the injury (e.g., burns, traumatic brain injury, splenic rupture), by the mechanism of the injury (e.g., motor vehicle, poisoning, firearm, explosion), and by the intent (e.g., unintentional, intentional, undetermined). If we classify by the nature of the injury, then we need to decide to analyze by the number of injuries or the number of injurious episodes or both, and the choice of the denominator would be critical. The mechanism and intent of the injury is useful in quantifying the problem of motor vehicle crashes, explosions, and such, and in using that information to improve triage and acute care strategies. However, explosions may not lead to physical injury in a particular individual. These incidents are important, though, since understanding the reasons why certain individuals were not injured may lead to improvements in protecting the physical environment and in helping health care systems predict how many persons will be seen in a particular time period for a given type of explosion. Unfortunately, the current state of collecting explosion-related injury data is disjointed, and data elements are varied in their level of collection and specificity. As a result, data collection procedures tend to be unstructured and prevent the ability to feasibly compare injuries across different explosion events. Finally, definitions of the nature of the injury can vary significantly. For example, there are no standard definitions of blast lung injury, mass casualty event, or terrorism-related injury. In this chapter, we will use the terms explosion-related injury and blast-related injury interchangeably.

Injuries that result from a blast are dependent on many factors, including the type of explosive and explosive charge, height of burst, reflecting boundaries or protective barriers, distance between the victim and the

blast, the surrounding environment, and the scattering of fragments or other projectiles. The physical environment in which an explosion occurs plays a significant role in the type and degree of injury that may result. Blasts that occur in an enclosed space (e.g., a closed room, bus, or subway car) can intensify the effect of the blast wave, resulting in more severe injury patterns than those that occur in open air (e.g., plaza, open market, train platform) (Kluger 2003; Leibovici et al. 1996). In addition, explosive events associated with building collapse result in higher mortality and morbidity (Frykberg 2002).

Common explosive blast injuries include pulmonary barotrauma, brain injury, abdominal hemorrhages, ocular injury, tympanic membrane rupture and middle ear damage, crush injuries, traumatic amputations, and burns. Blast injuries are the result of any of four basic mechanisms termed as *primary, secondary, tertiary*, and *quaternary*. Some researchers have suggested adding a fifth (*quinary*) mechanism. Victims may have complex injury patterns involving multiple organ systems as a result of a combination of some or all of these blast injury mechanisms (DePalma, Burris, Champion & Hodgson 2005). These mechanisms and the more in-depth epidemiological data will be described in more detail in subsequent sections in this chapter.

Epidemiology is the study of disease occurrence and its patterns in human populations, and of the determination of the factors that impact on those patterns (Lilienfeld & Lilienfeld 1980). As the field of injury prevention and control continues to grow and as new events unfold, new aspects present challenges that can be addressed through epidemiologic analyses. For example, the events of September 11, 2001 showed that the care of the acutely injured during a terrorist event is a critical role for public health, and that better, compatible data systems are needed to evaluate and improve the effectiveness of trauma care (Centers for Disease Control and Prevention [CDC] 2002a, 2002b; NCIPC 2005). Acquiring accurate data can be difficult, especially in mass casualty situations in which the epidemiologist does not control the experimental setting and data are not collected in a standardized manner. In an optimal system, one would like to have in-place standardized data collection so as to evaluate systems of care (e.g., response times, field triage, resource allocation, prehospital and hospital trauma components, communications), outcomes of care (mortality, morbidity, disability, mental health), and costs to the system

(financial, social, displaced persons, long-term care). Through this evaluation, we can improve our responses and care to those victims of explosions.

In this chapter, we will first delve into the methodological issues in obtaining useful epidemiologic data. Second, we will describe in detail the concept of the agent (mechanical energy from a blast) and its relationship to the human host and its interplay with the environment. Issues related to triage, management during hospitalization, and resource utilization after a blast will also be covered in that section. Third, we will describe the current epidemiologic data related to morbidity and mortality, and discuss other important concepts, to include those of critical mortality versus immediate and long-term mortality. We will conclude by putting each of these sections into perspective and detailing what will be needed to develop systems to collect standardized data within and among nations.

METHODOLOGICAL ISSUES

In the disaster setting, such as an explosion-related event, it is critical that terms are clearly and consistently defined. A *mass casualty event* exists when the numbers, severity, and diversity of injuries overwhelm local medical resources. In this situation, comprehensive and definitive care cannot be provided to all victims. This is in contrast with a *multiple casualty incident*, in which local resources are able to manage the number of casualties (Committee on Trauma, American College of Surgeons 2006). The term *surge* has been used to describe the large numbers of patients that present to the medical care system in a short time period. The ability of a medical system to absorb this sharp and sudden increase in volume is termed *surge capacity*.

Critical to comparing outcomes among injured patients is a valid system to classify the type and extent of injuries to those victims. In 1976, the Abbreviated Injury Scale (AIS) was published after its initial introduction by a consensus committee in 1971 and is now the most widely accepted and used severity scale worldwide. It was intended to be a standardized system for classifying the type and severity of injuries resulting from motor vehicle crashes, but its purpose has expanded in updated revisions to include burns, penetrating trauma, and other causes of injury. A new edition AIS 2005, which replaces AIS 98, has an expanded dictionary of

injury terms and diagnoses with increased specificity needed for categorizing severity and outcomes. AIS 2005 contains more than 2,000 injury descriptors that can be anatomically localized and now has a new section dealing with blast injury (Gennarelli & Wodzin 2006).

The AIS is used to classify each injury in every body region with a simple numerical score for ranking and comparing injury severity. Each injury is assigned an AIS score on an ordinal scale ranging from 1 (minor injury) to 6 (probably lethal/maximum injury) (see Table 1-1). An AIS of 6, however, is not equivalent to death of the individual, but with maximal injury to the organ.

AIS does not account for the combined effect of multiple injuries. Since there is not a linear association between maximal AIS and mortality, the injury severity score (ISS) was derived using the AIS scores as a basis. The ISS is also an anatomically based ordinal scale with a range from 1 to 75 (Baker, O'Neill, Haddon & Long 1974). To compute the ISS, the AIS scores are assigned to each of six body regions: head/neck; face; thorax; abdomen/visceral pelvis; bony pelvis/extremities; and external structures. The ISS then is calculated as the sum of the squares of the highest AIS scores in each of the three most severely injured body regions. Only one injury (most severe) per body region is used in the score. An AIS score of 6 in any body region is automatically assigned a maximal ISS of 75. Table 1-2 provides an example of the calculation of ISS.

The ISS correlates with mortality, morbidity, and hospital stay. ISS has been used to predict mortality, and has also been found to be a consistent risk factor predictor for postinjury multiple organ failure (Balogh, Offner & Moore 2000). In trauma research, the ISS also has been used to

Table 1-1 The Abbreviated Injury Scale (AIS)

AIS Score	Injury
1	Minor
2	Moderate
3	Serious
4	Severe
5	Critical
6	Probably Lethal[a]

[a] *A perfect linear correlation with an AIS of 6 and mortality does not exist, but survivability is low.*

Table 1-2 Example of the Injury Severity Score

Body Region	Injury	AIS[a]	Top Three Scores Squared
Head/Neck	No injury	0	
Face	Anterior epistaxis	1	
Thorax	Flail chest	4	16
Abdomen	Splenic rupture	5	25
Extremity	Femur fracture	3	9
External	Contusions	1	
Injury Severity Score			**50**

[a]*Abbreviated Injury Scale.*

dichotomize trauma patients into severe injuries (ISS >15) and into non-severe injuries (ISS ≤15), and to evaluate outcomes of patients with similar degrees of injury severity.

The ISS has several limitations. Because only one injury per body region can be scored, patients may be more seriously injured than reflected in the score. Similarly, limiting the scoring to three body regions does not take into account a more seriously traumatized individual with additional regions injured. As a result, ISS may underestimate seriousness of injury in victims of multiple penetrating trauma, such as in the case of explosion-related injuries. It also does not take into account physiologic status, age, or preexisting medical conditions. Several other scoring systems have since been devised to address these limitations, but which scoring system most accurately reflects injury severity remains controversial. Nonetheless, the ISS remains the most popular system described in the literature regarding explosion-related injury.

Optimal data systems for use in explosion-related events remain a challenge. It is essential that accurate and reproducible information be collected across the continuum of care. This information would then be available to evaluate care provided after an explosion, which could then result in improving injury and trauma care and subsequent long-term and mental health care. Unfortunately, there is a lack of standardized definitions and data and data collection practices within and across nations so that the experiences gained in each incident are of limited value in the preparedness planning of another. Furthermore, in mass casualty events, which by definition have resulted in an overwhelmed medical system,

the chaos accompanying the event is not an optimum environment for the nonpreplanned recording of accurate data from which relevant studies may be undertaken.

Standards need to be developed that include data elements, clinical vocabularies, and coding systems that convey information about the nature, severity, treatment, and outcomes of injuries. Data systems also need to be created that facilitate the sharing of information between nations and promote standard comparability of injuries across different bombing and explosion events. The utility in standard systems is the ability in comparing different bombing and explosion events, which can lead to significant changes in clinical and public health practice. Much of the data during bombing events that could be used to save lives in future events are not collected routinely due to lack of preplanning and the chaotic nature of the event. Finally, persons may not even be aware if certain data for specific bombings and explosion disasters exist. Because of lack of planning, data that should be collected immediately after the disaster, called perishable data, are never collected. These data might include information on demographics and injury types, which are needed to study the intermediate and long-term health effects of bombing-related injuries.

MECHANISMS AND CONSEQUENCES OF BLAST-RELATED INJURY

Health Care Challenges

The global terror threat exists during a time when the hospitals and emergency departments in the United States are having difficulty in providing timely, efficient care for patients on a daily basis. In 2003, there were 113.9 million patient visits to emergency departments (ED) in the United States, an increase of over 25% from 1993, and a decrease in the number of U.S. EDs by 14% (McCraig & Burt 2005). The problem worsened in the 1990s when the United States lost 103,000 staffed inpatient medical surgical beds and 7,800 intensive care unit (ICU) beds (American College of Emergency Physicians [ACEP] 2007). These reductions in EDs and hospital and ICU beds, combined with the near daily diversion of emergency medical services (EMS), personnel shortages, increasing nonemergency visits to EDs, and regionalized surgical care have led to the development of unparalleled crowding in EDs across the country (Derlet & Richards 2000; Eckstein et al. 2005; Schafermeyer & Asplin 2003; USGAO 2003b; American Hospital

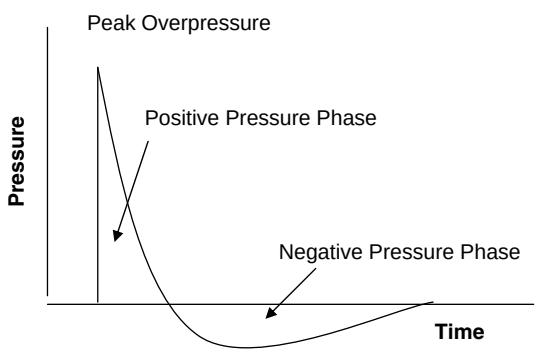
Association [AHA] 2002). In 2006, the Institute of Medicine released a report highlighting the challenges facing the nation's emergency medical care system (Institute of Medicine [IOM] Committee on the Future of Emergency Care in the United States Healthcare System 2006a; IOM, 2006b, 2006c).

When transporting patients to the hospital, EMS crews often are diverted from one facility to another due to overcrowding in the ED and hospital. According to a 2003 report from the National Center for Health Statistics, 34% of U.S. EDs diverted ambulances from primary destinations (Burt & McCraig 2006). Frequently, emergency medical technicians (EMTs) are forced to wait for extended periods in EDs before their patients can be transferred to hospital staff, hindering the care of the individual patient and impacting the EMS system's ambulance availability for additional calls. Patients are evaluated and treated in ED hallways, and may be held in the ED for extended times after they have been admitted (for hours, or even days) while they await an inpatient bed as health care facilities try to cope with high occupancy rates.

The Physics of Blast

Explosives may be categorized as either low-order explosives or high-order explosives (CDC 2003). Low-order explosives (gunpowder) release energy through a process called *deflagration*, which occurs at subsonic speeds, and is essentially a "burning" of the material (Langworthy, Sabra & Gould 2004). High-order explosive (C4, TNT) detonations result in the rapid transformation of the explosive material into a highly pressurized gas, which releases energy at supersonic speeds (Langworthy et al. 2004; Wightman & Gladish 2001; Horrocks 2001; Cullis 2001).

FIGURE 1-1
Idealized blast waveform.



Explosions are physical phenomena that result in the sudden release of energy; they may be chemical, nuclear, or mechanical. This process results in a near-instantaneous pressure rise above atmospheric pressure (Figure 1-1). This positive pressure peaks ("overpressure"), and then falls rapidly into a longer negative pressure phase before subsequently returning to baseline. The positive pressure rise compresses the surrounding medium (air or water) and results in the propagation of a blast wave, which extends outward from the explosion in a radial fashion (Langworthy et al. 2004; Cullis 2001; Sasser, Sattin, Hunt & Krohmer 2006; Elsayed 1997;

Yetiser & Ustun 1993; Mayorga 1997; Kluger 2003). As the front or leading edge of the blast wave expands, a decrease in pressure follows it with the development of an underpressure (negative) wave (Sasser 2001).

The aforementioned discussion and figure refer to explosions in an ideal, or free field, environment. If the explosion takes place in a confined environment (bus, subway, room), the blast wave becomes complex as it reflects off surrounding structures (Cullis 2001; Sasser et al. 2006; Elsayed 1997; Yetiser & Ustun 1993; Kluger 2003). This increases the total force of the positive pressure phase, prolongs the duration of this phase, and results in increasing injury severity.

Injury Patterns

The four basic types of blast-related injury are described in relation to the mechanism by which they occur, and have been termed primary, secondary, tertiary, and quaternary (or miscellaneous) (Cullis 2001; Kluger 2003; Shaham et al. 2002; Knapp, Sharp, Beatty & Medina 1990; Phillips 1986). *Primary* blast-related injuries are characterized by anatomical and physiological changes that result from the blast wave impacting the body's surface and tissues, and affect primarily gas-containing structures. *Secondary* blast-related injuries result from flying debris (e.g., glass, concrete, wood) and bomb fragments striking the victim, resulting in penetrating or less commonly blunt trauma. *Tertiary* blast-related injuries result from the victim being thrown by the blast wind (forced super-heated air flow), which can lead to fractures, traumatic amputations, closed and open brain injuries, or other blunt or penetrating trauma. *Quaternary* blast-related injuries are all explosion-related injuries, illnesses, or diseases not due to *primary*, *secondary*, or *tertiary* mechanisms and include exacerbation or complications of existing conditions. Examples include thermal or chemical burns, radiation exposure, or inhalation injury from exposure to dust or toxic gases. Some authors have suggested a fifth mechanism, *quinary* blast-related injury referring to a hyperinflammatory state out of proportion to the injury sustained (Mayo & Kluger 2006). Kluger (2003), recognizing that most victims of terrorist bombings have injuries caused by multiple mechanisms, uses the term *multidimensional injury*.

Primary Blast-Related Injuries

Primary blast injuries are the direct result of the impact of the blast wave upon the body. They are unique to high-order explosive detonations, and

present an injury pattern not typically seen outside of combat, thus making them unfamiliar to most civilian physicians (CDC 2003). Therefore, much of this discussion will focus on *primary* blast injuries, particularly blast lung injury.

As the blast wave impacts the body surface, a pressure differential is generated at the body surface that results in rapid acceleration and movement of the body surface and resultant propagation of shear and stress waves through the tissue (Wightman & Gladish 2001; Horrocks 2001). Previous concepts of spalling and implosion have not been borne out in animal studies, and the mechanism of injury most likely is due to tissue stress leading to mechanical failure and resultant injury, or "irreversible work." These waves result in direct tissue injury and primarily affect gas containing structures: ears, lungs, and gastrointestinal tract.

Tympanic Membrane Rupture

The tympanic membrane is the most commonly injured body structure after a blast (DePalma, Burris, Champion & Hodgson 2005) and may occur at relatively low pressures (5 PSI) (Mayo & Kluger 2006; Horrocks 2001). It was reported in 41% of patients seen at Gregorio Marañon University General Hospital (GMUGH) following the Madrid 2004 bombings (Gutierrez de Ceballos et al. 2005). It is not, as previously thought, a marker for more serious *primary* blast injury (Leibovici, Gofrit & Shapira 1999). Injuries predominantly affect the *pars tensa* (Horrocks 2001; Stein & Hirshberg 1999), and heal spontaneously in most cases. Patients may present with otalgia, bleeding from the ear, tinnitus, hearing loss, and otorrhea (Horrocks 2001; Phillips 1986).

Most tympanic membrane ruptures from blast injury are reported to heal spontaneously and thus management is typically conservative (DePalma et al. 2005). It has been reported that up to 25% of these patients will require surgical repair (Phillips 1986), especially those with large surface area affected (Kronenberg, Ben-Shoshan & Wolf 1993). A thorough examination should be performed and the patient referred for follow-up within 24 hours (Stein & Hirshberg 1999) for otorhinolaryngology (ENT) evaluation and audiometry (Health Protection Agency [HPA] 2005). Earlier involvement of an ENT may be necessary for debris removal from the canal (Wightman & Gladish 2001) or significant injuries. Irrigation should be avoided (Sasser 2001). Antibiotics may be indicated if there is significant

debris in the wound (DePalma et al. 2005), but should be done in consultation with ENT (HPA 2005). In a six-month follow-up of the U.S. embassy bombing in Kenya, Helling (2004) noted that five out of 14 tympanic membranes injuries with no prior intervention had failed to heal, and the author recommended early debris removal, eversion, and paper patches. Cholesteatoma is a potential late complication of this injury.

Abdominal Blast Injury

Blast injury to the abdomen is reportedly rare (Kluger 2003), with most injuries affecting the colon (Mayo & Kluger 2006; Stein & Hirshberg 1999) and occurring in underwater explosions (Argyros 1997). However, in a study involving 29 hospitalized patients from a bus bombing, it was reported that four of 29 (14%) patients had *primary* blast injury to the abdomen (Katz et al. 1989). Injuries may include contusion, hemorrhage, bowel perforations, and ischemia (Wightman & Gladish 2001; Horrocks 2001; Stein & Hirshberg 1999; DePalma et al. 2005). Depending upon the specific injury, the presentation of abdominal blast injury may be delayed (CDC 2003). Patients may present with abdominal pain, nausea and vomiting, diarrhea, tenesmus, and rectal bleeding; signs may include hemodynamic instability, abdominal guarding, peritoneal irritation, and rectal bleeding (CDC 2003; Argyros 1997). Injuries to solid organs are likely the result of *secondary* or *tertiary* mechanisms (Kluger 2003). The management of patients with suspected primary abdominal blast injuries may include observation, reassessment, radiography (plain and computerized tomography [CT]), and operative intervention.

Blast Lung Injury

Pulmonary injury, or blast lung injury, is a result of the blast wave's impact upon the thorax, and is a significant cause of death both at the scene of explosion, and in initial survivors (Cooper et al. 1983; Frykberg & Tepas 1988; Stein & Hirshberg 1999; Hadden, Rutherford & Merrett 1978). Classically described as pulmonary injury occurring without obvious injury to the chest, this may be difficult to distinguish in the multiply injured bombing victim. In a large review of 220 terrorist bombings, Frykberg and Tepas (1989) reported a 47% incidence in blast lung injury in immediate fatalities. Katz et al. (1989) reported that 38% of victims hospitalized following a civilian bus bombing were diagnosed with blast lung injury. In the March 2004 terrorist bombings in Madrid, 17 of 243 (7%)

patients seen at GMUGH were diagnosed with blast lung injury. However, Gutierrez de Ceballos et al. (2005) noted that *primary* blast injury to the lung was present in 63% of critically ill ICU patients.

Blast lung injuries result in severe pulmonary injury characterized by contusion, hemorrhage, and edema with both alveolar and vascular injury (Knapp et al. 1990; Phillips 1986; Pizov et al. 1999; Tsokos et al. 2003; Hirshberg et al. 1999; Frykberg, Tepas & Alexander 1989), and seem to be related to the pressure differentials produced at tissue surfaces of different densities (Mellor 1992). Pneumothoraces, hemothoraces, bronchopleural fistulas, alveolar pulmonary venous fistulas with resultant air embolization, fat embolization, and other thoracic injuries may also be present.

Patients with blast lung injury may present with a broad spectrum of respiratory symptoms (chest pain, hemoptysis, difficulty breathing, cough) and/or signs (tachypnea, hypopnea, apnea, cough, hemoptysis, altered lung sounds, hypoxia). Additionally, Almogy et al. (2006) reported that patients who had more than 10% body surface area burns, skull fractures, and penetrating torso or head injuries were more likely to have blast lung injury.

Patients in whom the diagnosis of blast lung injury is being considered should receive supplemental oxygenation to prevent hypoxia and may require further interventions to secure their airways and to ensure adequate oxygenation and ventilation (intubation, tube thoracostomy). Chest radiography may reveal the characteristic "butterfly" pattern seen in blast lung injury (Katz et al. 1989; Stein & Hirshberg 1999; Hirshberg et al. 1999) or reveal evidence of additional thoracic injury. For those who require endotracheal intubation and mechanical ventilation, applying permissive hypercapnia, with alveolar hypoventilation and low peak pressures, may help avoid the risk of air embolism due to pulmonary tissue damage (Frykberg 2002; Stein & Hirshberg 1999; Sorkine et al. 1998). Fluid administration in the patient with blast lung injury should be judicious, ensuring adequate tissue perfusion but avoiding fluid overload (Sasser et al. 2006). Patients diagnosed with air embolism should be placed in the prone, semi-left lateral, or left lateral decubitus position (Wightman & Gladish 2001; Argyros 1997; Lavonas & Pennardt 2006) and transferred to a hyperbaric chamber for further treatment.

Patients diagnosed with blast lung may require aggressive, complex management, and should be admitted to an ICU (Shaham et al. 2002).

Patients in whom blast lung injury is suspected, based on specific complaints or physical findings, should be observed in the hospital. There are, however, no definitive guidelines for observation, admission, or discharge of patients with the potential for primary blast lung injury following an explosion. Patients who have no complaints or findings suggestive of blast lung injury, no hypoxia, and normal plain chest radiographs, may be considered for discharge, with strict instructions, after a brief observation period (6–8 hours) (Sasser et al. 2006).

Traumatic Brain Injury

Traumatic brain injury, thought to be due primarily to *secondary* or *tertiary* mechanisms, is increasingly seen as having a significant *primary* blast injury component (CDC 2003; DePalma et al. 2005; Okie 2005; Guy, Glover & Cripps 2000), and patients with this injury may have behavioral and cognitive dysfunction.

Secondary Blast-Related Injuries

Secondary blast-related injuries include penetrating and blunt trauma due to projectiles and flying debris. These injuries often result in lacerations, fractures, and contusions, and along with *tertiary* injuries account for the majority of injuries seen in survivors. In the Khobar Towers bombing, 95% of all injuries seen were soft tissue injuries, with most due to *secondary* mechanisms, and treated in the outpatient environment (Thompson et al. 2004). There is often extensive wound contamination (Frykberg & Tepas 1988; Halpern, Tsai, Arnold, Stok & Ersoy 2003) with *secondary* blast injuries, and the use of fragments (nuts, bolts, nails) in bombs by terrorists has resulted in patients with multiple penetrating injuries, making prioritization and management of these patients a challenge (Kluger 2003; Gutierrez de Ceballos et al. 2005; Almogy et al. 2004). Observation, reassessment, a high index of suspicion, and aggressive use of radiography and other diagnostic modalities is mandatory for these patients. Of note, ocular injuries may be significant. Eight percent of the injured survivors in Oklahoma City sustained an eye injury; of these, 29% were greater than 300 feet from the blast (Mines, Thach, Mallonee, Hildebrand & Shariat 2000).

Tertiary and Quaternary Blast-Related Injuries

Tertiary injuries are the result of physical displacement of the victim, with rapid acceleration and deceleration, resulting in blunt force trauma

(Einav, Aharonson-Daniel, Weissman, Freund & Peleg 2006). The category termed *quaternary* injuries, also referred to as miscellaneous injuries, contains injuries secondary to burns, structural collapse, toxins and inhalations, and exacerbation of chronic disease (CDC 2003; Phillips 1986). The vast majority of these injuries will be managed according to established protocols. Of note, crush injuries due to structural collapse of a building have been termed both a *tertiary* (Mayo & Kluger 2006; Horrocks 2001; DePalma et al. 2005) and a *quaternary* injury (CDC 2003; Phillips 1986; Stein & Hirshberg 1999; Einav et al. 2006).

Planning and Resource Utilization

Shapira et al. (2006) reported that 86% of casualties, who die from a suicide bombing, die at the scene. In an analysis of 29 terrorist bombings that resulted in 8,364 casualties, Arnold, Halpern, Tsai, and Smithline (2004) reported that different bombing scenarios (structural collapse, confined space, or open space) produced different numbers of surviving casualties and subsequent hospitalizations. Structural collapse bombings resulted in the highest number of injuries (median 359) and hospitalizations (median 85). In contrast, confined space explosions without structural collapse resulted in fewer survivors (median 53) and hospitalizations (median 25). Open space explosions produced a median of 76 survivors with 18 hospitalizations (Arnold et al. 2003).

In a review of 325 victims from 32 events in Israel, Einav et al. (2006) noted that the average number of patients who arrived in the ED was 20.9, with an average of 10.9 patients admitted per event. Of those admitted, 39.7% underwent a CT scan and 60.3% had an operative procedure. In that same study, which involved an examination of multiple casualty incidents involving the care of injured patients from suicide bombings at Level I trauma centers in Israel, the authors concluded that hospital planning must account for the significant overlap in the personnel resources required for the ED, ICU, and operating rooms (OR), anticipate radiology and inpatient bed (particularly ICU) demands, and prepare the surgical services to handle a continuous OR load for over 24 hours. Hospitalization rates have been reported to range from 13% for open air bombings, to 52% for confined space bombings, and 58% for suicide bombings. Halpern et al. (2003) identified radiology (including plain film and CT) as a bottleneck in the care of patients in the ED.

A terrorist bombing and the resultant surge of casualties has the potential to rapidly stress the capabilities and function of any hospital, especially when hospitals are currently operating at or above capacity. Many hospitals currently are not prepared to handle bombing victims. Despite this fact, a CDC publication determined that explosive events were addressed in about three-fourths of hospital disaster plans, but few (one-fifth) had conducted a drill with a scenario involving explosives (Niska & Burt 2005).

Field Triage in Terrorist Bombings

There are multiple proposed mechanisms and algorithms for the field triage of disaster patients; however, there is very little evidence to support one methodology over another (Cone & Macmillian 2005) and there remain many challenges to disaster research (Auf der Heide 2006). At its core, triage in disasters, including terrorist bombings, seeks to "identify the critically injured patients who need immediate care, providing them with lifesaving procedures and transporting them to the surrounding hospitals after considering their capabilities and avoiding overcrowding of any of them." (Kluger 2003) With this goal in mind, much of the planning with regard to the emergency medical response to terrorism assumes that the existing system will function to support and achieve this outcome. However, in a review of the literature, Auf der Heide (2006) reported that the actual response during a disaster is often quite different from preparedness and planning assumptions. It involves uncoordinated dispatch, lack of hospital notification and communication, significant bystander involvement and rescue, absent or ineffective scene triage, self-referral, and the transport of many, if not most, patients to the nearest healthcare facility. As a result, hospitals receive the least-injured patients before the critically injured, impacting effective triage, transportation, and distribution of injured patients. As examples:

- Following the July 2005 bombings in London, the Royal London Hospital, which received 194 casualties, reported that all communications with the scene failed, and there was no information about reported casualties (Aylwin, Konig & Brennan 2006).
- In the bombing of the Murrah Federal Building in Oklahoma City in 1995, over 60% of the patients went to hospitals within 1.5 miles of the event site; the majority of patients (more than 65%) were not transported by formal emergency medical services

systems. Victim extrication was performed by a combination of victims, lay personnel, and trained rescuers (Mallonee et al. 1996).

- In the aftermath of the 2004 Madrid bombings, GMUGH evaluated 272 patients in 2.5 hours, with the first patient arriving on foot 17 minutes after the last explosion (Gutierrez de Ceballos et al. 2005).

Effective triage and patient distribution is imperative, and requires that system planners recognize both the experiential base from prior events and the limited evidence base for triage methodology, and adapt their local plans accordingly. In repeated bombing events, the overtriage of patients has been shown to correlate directly with the mortality of those patients who were critically injured in the event (Frykberg & Tepas 1988; Frykberg 2002).

MORBIDITY AND MORTALITY

Overview

Most terrorist attacks involve explosions and bombings. Data collected by the Terrorism Research Center[1] revealed 759 terrorist attacks for the year 2005, of which 399 (53%) were associated with explosions. Furthermore, explosions and bombings remain the most common man-made cause of disasters resulting in large numbers of casualties (Frykberg 2002). Analysis from the Terror Attack Database[2] from 1991 to 2000 found that 88% of terrorist attacks involving 30 or more casualties were caused by explosions (Arnold et al. 2004).

[1]The Terrorism Research Center is an independent institute dedicated to the research of terrorism, and compiles a list of terrorist events in a worldwide media watch. It can be accessed through their web site at www.terrorism.com.

[2]The Terror Attack Database is a project of the International Policy Institute for Counter-Terrorism. It can be accessed on their web site at www.ict.org.il.

Importance of Surveillance

After road traffic, suicide, and violence-related deaths, war-related injuries were, in 2000, the fourth leading injury cause of death among persons aged 5 to 44 years globally, and virtually all these deaths occurred in low- and middle-income countries (Peden, McGee & Krug 2002). In 2002, the number of war-related deaths were about 171,000 (World Health Organization, Department of Measurement and Health Information 2004). Deaths, however, represent a fraction of the war and terrorism-related injury problem, as for every person killed many more survive and live with the direct (e.g., disability) and indirect (e.g., social, economic) consequences of these events (CDC 1997; Krug et al. 1998; Andersson et al. 1995; Ascherio et al. 1995; Aschekenasy-Steuer et al. 2005; Mallonee et al. 1996).

Although the consequences of bombs and other explosive devices (e.g., landmines) have been documented (CDC 1997; Krug et al. 1998; Andersson et al. 1995; Ascherio et al. 1995; Aschekenasy-Steuer et al. 2005; Mallonee et al. 1996; Shamir, Rivkind, Weissman, Sprung & Weiss 2005), much is still needed to learn about the impact of these events on the health, social, and economic status of affected populations. For example, more precise data are needed about those who acquire secondary pneumonia after a severe blast-related injury to the lung (Aschekenasy-Steuer et al. 2005; Shamir et al. 2005) and those who develop long-term psychological consequences of terrorism, in particular post-traumatic stress disorder (PTSD) (Shalev 1992; Desivilya, Gal & Ayalon 1996).

Identifying ways to prevent or reduce vulnerability to these types of events requires an understanding of the epidemiology of explosion-related injuries, and therefore requires surveillance data.[3] Surveillance data are analyzed to determine the magnitude, scope, and characteristics of a health problem; to study the factors that increase the risk of disease, injury, or disability; to determine which risks are potentially modifiable; to assess what can be done to prevent the problem using the information about causes and risk factors; to design, pilot test, and evaluate interventions, and to then implement the most promising on a broad scale (Krug et al.,1998; Holder et al. 2001). A surveillance system should include a functional capacity for data collection, analysis, and dissemination linked to public health programs (Holder et al. 2001).

Challenges to Data Collection and Analysis

Although explosion-related injury surveillance has been conducted in several settings (Ascherio et al. 1995; Aschekenasy-Steuer et al. 2005; Mallonee et al. 1996; Rodoplu et al. 2005; Leiba et al. 2005; Shamir et al. 2005), these efforts, especially in areas of conflict or war, often are limited in scope, inconsistently implemented, or hospital-based and do not account for persons killed or injured who never reach a hospital. Countries need to implement or expand the scope of their population-based general injury surveillance systems or periodic cross-sectional surveys, and collect data in a consistent manner using standardized minimum data collection instruments and definitions (Sethi & Krug 2000; Physicians for Human Rights 2000). Collecting uniform data is essential to generate reliable intra- and intercountry comparisons of injuries from explosions.

[3]Surveillance is the ongoing, systematic collection, analysis and interpretation of health data essential to the planning, implementation, and evaluation of health practice, closely integrated with the timely dissemination of these data to those who need to know (Holder 2001).

During times of emergency, developed nations have implemented mandatory reporting of explosion-related injuries (Mallonee et al. 1996). After the 1995 Oklahoma City bombing, this mandate greatly enhanced access to data and medical records from multiple sources (e.g., medical examiner, hospital, and ambulance records; media reports), allowing the ascertainment of the risks and the number of persons at risk for severe events (e.g., building collapse) (Mallonee 1996). Data collected through this integrated approach can be used to make the case for the design of safer buildings (e.g., recommending the use of blast-resistant materials such as tempered glass and window coverings), improve evacuation plans, and to plan the allocation of medical and rescue resources and operations (e.g., ambulances, blood supply). Public health agencies need to develop or enhance such surveillance systems, analyze and link the findings to the management decision process (Noji 2000), and disseminate the data collected to improve the level of preparedness in countries or regions affected by conflict or war.

Concepts of Mortality

In contrast to the classic triphasic distribution of mortality seen in standard blunt and penetrating trauma, mortality from explosions results in a biphasic distribution; there is a high immediate mortality rate, followed by a low early and late mortality rate. Immediate mortality rates are affected by many factors, including magnitude of the explosion, proximity to potential victims, presence of building collapse, and closed versus open space environment. In a study of 29 mass casualty bombings, Arnold et al. (2004) found that immediate mortality was one in every four persons for bombings with structural collapse, one in every 12 persons in confined space bombings, and one in every 25 persons in open air bombings.

Most survivors of explosions have noncritical or no injuries. As a result, the low overall mortality rate among the injured is deceiving. A more informative rate is the *critical mortality rate*, which is the mortality rate among the subgroup of critically injured survivors. A *critical injury* may be defined as one in which a casualty presents with an acute airway, breathing, circulatory, or neurological problem that requires immediate surgical intervention, admission to the ICU, and/or endotracheal intubation (Gutierrez de Ceballos et al. 2004). The critical mortality rate is more indicative of the severity of the event and of the results of medical management rendered, and typically ranges from 9 to 22% (Frykberg 2002). In compiling the results of ten terrorist bombing incidents, Frykberg found a linear relationship

between the critical mortality rate and the rate of overtriage, which is the percentage of patients with minor injuries but classified as needing immediate treatment. In his study, overtriage ranged from 8 to 80% (averaging 53%) and critical mortality ranged from 0 to 37% (averaging 12.6%); the linear correlation coefficient was an extremely high $r = 0.92$.

Patterns of Injury and Mortality

The environment of the bombing is an important determining factor in the mortality and severity of injuries (Leibovici et al. 1996). There are distinct patterns that may be noted regarding these events: most injuries will likely be minor (Frykberg & Tepas 1988); most injuries seen in survivors of a bombing will be due to *secondary* and *tertiary* blast mechanisms (Cooper et al. 1983; Frykberg 2002; Brismar & Bergenwald 1982); explosions in a confined space result in a higher incidence of *primary* blast injury, including lung injury (Horrocks 2001; Leibovici et al. 1996; Katz, Ofek, Adler, Abramowitz & Krausz 1989; Pizov et al. 1999); traumatic amputation is rare in immediate survivors, is commonly noted in fatalities at the scene, and indicates close proximity to the blast (Horrocks 2001; Stein & Hirshberg 1999); and structural collapse results in a higher number of immediate deaths (Frykberg 2002; Halpern et al. 2003). There have been multiple bombing analyses reported in the medical literature that provide general information about the patterns of death, hospitalization, and outpatient treatment following a bombing (see Table 1-3).

Table 1-3 Patterns of Death, Hospitalizations, and Outpatient Treatment following a Bombing Event

Author	Total Injured No.	Deaths No. (%)	Admitted No. (%)	Outpatient No. (%)
Mallonee et al., 1996	759	167 (22)	83 (11)	509 (67)
Thompson, Brown, Mallonee & Sunshine, 2004	420	19 (5)	66 (16)	335 (80)
Cooper, Maynard, Cross & Hill, 1983	385	28 (7)	104 (27)	253 (66)
Frykberg & Tepas, 1988	3357	423 (13)	881 (26)	2053 (61)
Biancolini, Del Bosco & Jorge, 1999	286	84 (29)	41 (14)	161 (56)

Table 1-4 Place of Explosion, Mortality, and Injury Severity[a]

Selected Characteristic	Open Space (%)	Enclosed Space (%)
Mortality	2.8	15.8
ISS >15	6.8	11.0
Multiple injury	4.7	11.1
Surgery required	13.5	17.6
ICU required	5.3	13.0

[a]*Adapted from Kluger, Y. (2003). Bomb explosions in acts of terrorism-detonation, wound ballistics, triage, and medical concerns.* ***Israel Medical Association Journal*** **5**, 235–240.

The increased incidence of *primary* blast injuries in enclosed spaces results in a much higher immediate mortality and in more critical injuries (see Table 1-4).

Leibovici et al. (1996) studied two open air and two enclosed space (bus) bombings. In each incident, the bomb was of similar size and constituents, and the victim density at close range was similar in all attacks. The difference in mortality was highly significant, with 49% dying in the enclosed space group and 7.8% in the open air group. The confined space group had more than double the victims with ISS greater than 15. Among hospitalized patients, 78% of the enclosed space group and 34% of the open air group had *primary* blast injuries.

Casualties of bombings are more severely injured and have more complex injuries than victims of conventional trauma (Peleg, Aharonson-Daniel, Michael & Shapira 2003). Kluger, Peleg, Daniel-Aharonson, and Mayo (2004) examined the Israeli National Trauma Registry and compared 906 terrorist bombing victims to 55,033 nonterror trauma victims that were hospitalized in 12 trauma centers from 2000 to 2003 (see Table 1-5). He found a significant difference in these groups in that the bombing casualties had higher ISS scores, lower Glascow Coma Scale (GCS) scores, higher frequency of hypotension on admission, greater number of body regions injured, greater frequency of ICU admission, higher incidence of surgical procedures, greater mortality rate, and greater need for rehabilitation services. Furthermore, explosion-related casualties are more likely to have more than three body regions injured than are conventional trauma patients (10.7% versus 1.5% in this study). Therefore, it is likely that victims of explosions are more severely injured than their ISS score would indicate. Frykberg (2002) identified eight prognostic factors for injured victims of

Table 1-5 Characteristics of Victims of Terrorist Bombings and of Conventional Trauma[a]

Variable	Terrorist Bombings (%)	Other Trauma (%)
ISS >15	28.7	10.0
GCS <6	9.5	2.9
Admission BP <90 mmHg	6.2	2.5
ICU admission	26.0	7.1
Body regions injured ≥3	28.3	6.2
Surgical procedure	50.8	36.6
In-hospital mortality	6.1	2.0

[a]*Adapted from Kluger, Y., Peleg, K., Daniel-Aharonson, L. & Mayo, A. (2004). The special injury pattern in terrorist bombings. Journal of the American College of Surgeons* **199**, 875–879.

bombings: magnitude of the explosion; building collapse; immediacy of medical care and treatment; triage accuracy; time interval to treatment; indoor versus open air explosion; urban versus rural setting; and anatomic injuries.

Immediate mortality is the result of combined blast, ballistic, and thermal effects on the body. Although the cause of death is usually evident, some victims have no readily identifiable mechanism. It is thought that air emboli or cardiac dysrhythmias may be the cause in such cases. In a study of over 800 victims from explosions in Northern Ireland, 14% died of complete body disruption, 39% had multiple injuries, 21% had head and chest injuries, 12% had only head injuries, and 11% had only chest injuries (Mellor & Cooper 1989). In another study of 305 fatalities from bombings in Northern Ireland, the top five pathological diagnoses among the deceased were brain injury (66%), skull fracture (51%), blast lung injury (47%), tympanic membrane rupture (45%), and liver laceration (34%) (Hill 1979).

The Walking Wounded and Severely Injured Survivors

Because a terror attack can occur anywhere and anytime, hospitals (even those across borders in areas of conflict or war) should be able to respond to a multiple casualty terror attack (Mallonee et al. 1996; Aschkenazy-Steuer et al. 2005; Leiba et al. 2005). Understanding the potential impact of explosions and terrorist bombings is critical for hospital emergency planning and preparedness (Mallonee 1996; Rodoplu et al. 2005).

Many factors may affect the number and arrival times of explosion-related injury victims to a hospital. These factors include the environment of the bombings (open-air versus confined space), the magnitude/size of the explosives; the number of explosions; proximity to the explosions; the mechanism of delivery of the explosives (e.g., person versus truck); the timing and day of the week of the attack; the proximity of the explosion to buildings and vehicles (more injury from flying glass or secondary explosions); the availability of field triage; the existence of a coordinated ambulance distribution center; the distance between the scene and the hospital; and the number of hospitals available (Aschkenazy-Steuer et al. 2005; Gutierrez de Ceballos et al. 2005; Shamir et al. 2005; Rodoplu et al. 2005; Leiba et al. 2005; Aylwin et al. 2006).

The initial arrival time to medical treatment of casualties after a terrorist attack ranges between 20 to 60 minutes (Aschkenazy-Steuer 2005; Leiba 2005; Gutierrez de Ceballos 2005). The Israeli experience indicates that survivors may arrive as fast as 18 patients in 6 minutes (Shamir et al. 2005; Shamir et al. 2004; Almogy et al. 2004).

The number of victims who arrive at a hospital varies by event. In the two open-air mass casualty bombings of 2003 in Turkey (no structural collapse), a total of approximately 483 persons were injured; the average of 242 per explosion is substantially higher than the median of 94 reported in other open-air mass casualty events (Rodoplu et al. 2005). One of the hospitals that responded to these attacks received 184 survivors (38% of all victims). All of them arrived within the first hour after the explosions; 88 (48%) of them were transported by ambulance and 96 (52%) arrived using alternate means (e.g., taxi, police cars, walking) (Rodoplu et al. 2005). In the open-air mass casualty bombing of 1995 in Oklahoma City (with structural collapse), a total of 759 persons were injured; of these, 162 (22%) died at the scene, 351 (47%) were treated in emergency departments as outpatients, 158 (21%) were seen in private physician offices, and 83 (11%) were hospitalized (Mallonee 1996). The multiple train bombings of Madrid in March 2004 (confined-space type explosions) resulted in approximately 2,062 victims; of these 177 (9%) died on the scene, 976 (47%) received medical care in 18 different hospitals (or 54 per hospital), 250 (12%) were treated in field hospitals, and 204 (10%) in primary health care clinics (Rodriguez & Serra 2005).

Although the number of victims and arrival patterns to hospitals vary (Shamir et al. 2005; Gutierrez de Ceballos et al. 2005), hospitals must

have plans in place to rapidly increase surge capacity in anticipation for a bombing event. This is especially true for acute care medical facilities located in areas of conflict or locales at risk for bombings. Given prior events, health care providers can expect casualties to arrive within 20 minutes of the bombing, with a majority of the total victims presenting for care within two hours.

Hospital Admission and Survival Rates

Many factors affect the number of hospital admissions and rates of survival. In addition to the factors just mentioned, the availability of hospital resources (e.g., operating theaters, number of intensive-care beds, medical specialty care) is also critical.

In the 2003 bombings in Turkey, of the 184 survivors seen in a hospital with a level I trauma center, 85% were discharged home within 12 hours after arrival, 21 (12%) were hospitalized, and seven (4%) with severe eye injuries were transferred to hospitals with ophthalmology services (Rodoplu et al. 2005). Eleven of the hospitalized cases (40%) required operative care and seven (4%) were critically wounded; of this latter group, three died. These figures were consistent with previous open-air mass casualty bombings (Rodoplu et al. 2005; Arnold et al. 2004; Leibovici et al, 1996; Walsh, Pracy, Huggon & Gleeson 1995). In the 1995 Oklahoma City bombing, of the 83 hospitalized survivors, two died (3% in-hospital death); one death was due to head trauma, and the other from multiple injuries, sepsis, and multiorgan failure (Mallonee et al. 1996). Aggregated data for victims of the 20 major bombing attacks (more than 10 persons wounded in each event) that occurred from 2001 to 2004 and were treated in the only level I trauma center in Jerusalem, Israel, indicate that 1,475 persons were wounded in these attacks (approximately 70 victims per event). Of these 1,475 persons, 477 (32%) were admitted to the emergency department (about 24 per event), 176 (12%) were hospitalized (about 9 per event); 92 (6%) were admitted to ICUs (about 4 per event), and only 11 died while hospitalized (Aschkenazy-Steuer et al. 2005). Of the 976 victims who were seen in 18 Madrid hospitals as a result of the multiple train bombings of March 2004, 509 (53%) were hospitalized 24 hours or more (about 28 per hospital), 458 (47%) were discharged the day of admission (about 25 per hospital), and nine (1%) died immediately after admission.

Of note, in contrast to these aggregated numbers, two of the 18 hospitals provided care to approximately 580 of the 976 victims (60%) (Rodriguez

& Serra 2005); reasons for this unequal distribution in at least one of the hospitals included its proximity to the place were the explosions occurred, easy and rapid access, and reputation as a reliable care provider (de Paula Rodriguez Perera 2005). The size and resources of this closest hospital, GMUGH, to the bombings in Madrid (1,800 beds, 40 ORs, and more than 40 ICUs) had a decisive role in the response; the availability of these resources, however, is an exception rather than the rule (Gutierrez de Ceballos et al. 2004; Turegano-Fuentes & Perez-Dias 2006). The experience of the multisite Madrid bombings suggests that reducing errors of field triage may enhance surge capacity by increased utilization of other available hospitals (Turegano-Fuentes & Perez-Diss 2006).

Estimating the number of victims arriving at a hospital and the expected arrival times, and developing and implementing preparedness plans that include procurement of all necessary resources (personnel, supplies) to respond to bombings will greatly reduce morbidity and mortality (Aylwin et al. 2006).

Long-Term Consequences Including Disability and Post-Traumatic Stress Disorder

The nature and severity of the medical consequences of bombings and explosions differ greatly from injuries seen in conventional trauma and have resulted in a new class of casualties (Peleg et al. 2004; Kluger et al. 2004). Bombings affect more young people, and produce more severe and complex injuries compared with those of nonterror trauma (Peleg et al. 2004; Kluger et al. 2004). In addition to consuming more resources acutely (e.g., surgical interventions, intensive care admissions), bombing casualties have longer hospital stays, experience greater disability, and require prolonged rehabilitation interventions and services (Sibai, Shaar & Yassir 2000; Kluger et al. 2004; Peleg et al. 2004; Arnold et al. 2004).

The clinical consequences of bombings and explosion-related injuries vary according to several factors. Some of these factors include length of evacuation time, capability to access timely and adequate medical care, and the ability of health care providers to implement pre-event strategies to cope with the event (Ryan & Montgomery 2005; Redhead, Ward & Batrick 2005). Other factors pertaining to the individual include the organ injured, the severity of the injury to the affected organ, and the number of body parts injured. A follow-up study of persons who experienced

blast-related lung injury indicated that most of the patients who survived regained pre-injury lung function within a year (Hirshberg et al. 1999).

Few studies have described the long-term consequences of bombings and explosion-related injuries. A study of civilians wounded during the 1996 Lebanon War indicate that approximately 25% of the survivors experienced a self-care related disability (e.g., eating/drinking, bathing, dressing, using toilet, housekeeping) and 38% sustained a motor-related disability (e.g., locomotion, lifting/carrying) (Sibai et al. 2000). This study also examined the relationship between the body part injured and resulting impairment/disabilities, in addition to the social impact of these events. Impairments were associated with injuries to the lower limbs, face, and abdomen. Motor-related disabilities were associated with injuries to the lower limbs and abdomen, as were disabilities in personal self-care. The social impact of bombings was also cited. Among the 55 survivors who were attending school, 29% were unable to resume after the event; and, of the 113 survivors who were employed before the event, 42% were unable to resume working (Sibai 2000).

Initially described in wartime combatants, post-traumatic stress disorder (PTSD) now is recognized as a common health problem associated with exposure to natural catastrophes, motor vehicle crashes, and violence, including terrorist attacks (de Jong et al. 2001; Kessler, Sonnega, Bromet, Hughes & Nelson 1995; Yehuda 2002). Estimates of the prevalence of PTSD after terrorist attacks range from 7.5 to 50% in the year following the event (Shalev 1992; Amir, Weil, Kaplan, Tocker & Witztum 1998; North et al. 1999). A study of 196 survivors of the 1995–1996 bombings in France found an overall prevalence of PTSD of 31.1% up to 2.6 years after the event (Verger et al. 2004); this reported PTSD prevalence is substantially higher than the 18.1% prevalence reported in victims of the 1982 and 1987 bombings in France. Although studies have reported that the prevalence of PTSD after a traumatic event declines with time, Verger et al. (2004) found that one-third of respondents did not have a remission in the 10 years following onset. They also found that PTSD was significantly higher among women, persons aged 35–54 (odds ratio (OR) = 2.83), those with severe initial injuries (OR = 2.79), those with cosmetic impairment (OR = 2.74), and those who perceived substantial threat during the attack (OR = 3.99). Some of these findings, however, are not fully supported by previous literature (Gibbs 1989). Verger also

indicated that survivors with moderate and mild injuries had a higher prevalence of PTSD (27.2% and 26.0%, respectively) compared with the general population (Kessler, Sonnega, Bromet, Hughes & Nelson 1995), suggesting that factors other than those associated with physical trauma (e.g., perceived threat) may play a role in the development of PTSD. PTSD may also be associated to factors such as the threat of death, or the viewing of mutilated bodies (Verger et al. 2004; Yehuda 2002; Baum et al. 1993).

As war and terrorism are widespread in the world, a better characterization of the epidemiology of the physical, psychological, and social consequences of bombings and explosions is needed in both civilian and military populations. This information will help health care providers, relief organizations, and planners to seek the means to provide appropriate medical, mental health, and rehabilitative services to survivors in order to minimize impairments and disability.

CONCLUSION

Explosion-related injuries due to terrorism represent an increasing burden to society. This burden can be considered in several ways: by incidence, defined as total, or fatal versus nonfatal; by incidence rates; or by total costs, defined by medical costs, losses in productivity, and increasing societal costs in improving security and protection. All of these burdens are increasing as the impact of terrorism continues to spread globally. Losses in functional and social capacity and reductions in quality of life for injured surviving individuals and their caregivers also add to this burden. It is not merely survival after an explosion-related injury that is important, but rather the ability of the individual to attain maximum physical recovery, to survive financially, and to enable secure, productive lives regardless of functional status.

We have learned a great deal over the last decade on how to care for the explosion-related victim, but, clearly, we have significant obstacles in learning how to maximize care and protect the public. Without accurate, uniformly defined information collected across the continuum of care, the determination and evaluation of which interventions are most effective in reducing the burdens will be difficult. Collecting these standardized data will be critical to changing medical practice as terrorist tactics and weapons change.

Few physicians and other health professionals have cared for victims injured by bombings. The average number of penetrating wounds in victims from an explosion is often much greater in the bombing victim compared with the routine trauma victim. The ability to push out key information on best practices quickly and efficiently to health professionals who are suddenly faced with a situation with which they are not familiar will be essential to optimizing care. Disaster planning and drilling, including how to acquire the key information, should be carried out regularly to identify weak points in those plans and to test alternative strategies.

Much work needs to be done to improve care and reduce the consequences of explosion-related injuries. It is critical for researchers to carry out more studies to identify interventions that can reduce these injuries and their adverse health effects. A major step forward would be to resolve questions about terminology and classification systems, make decisions about linking disparate systems, and determine which data should be collected during a disaster situation. International work groups should be convened to work on these issues. For example, a data module could be created that would collect minimum critical information. This data module would be consistent internationally so that data could be combined from multiple sites and analyzed to provide greater power in determining optimal care. Additional modules could be created for those facilities that want to carry out more in-depth analyses.

Finally, a need exists to improve communication between authorities and emergency departments and also between media and emergency departments during times of disaster. Patients not involved in the disaster will continue to have their emergent events, such as a myocardial infarction, acute asthmatic episode, or childbirth. Improving communication with authorities and the media on how to handle the increased volume of patients with routine and emergent care issues is needed so that these persons do not overburden the key disaster facilities while allowing appropriate triage of these nondisaster victims to other facilities.

Much concern remains about how best to provide care to injured victims in mass casualty situations. The impact of these events upon already fragile, overburdened, and underfunded or nonexistent systems of trauma care for operations, surge capacity, staffing, and logistical concerns is unknown but will clearly be far-reaching. Health care providers equipped

with the best data available can serve an important role in evaluating how these systemic effects of mass casualties impact the care of the injured victim. Local insight, effective partnerships, and analyses of internationally uniform data should lead to significant improvements in the outcomes of injured victims from explosions.

DISCLAIMER

The views, opinions and/or findings contained herein are those of the authors and should not be construed as an official position, policy , or decision of the Centers for Disease Control and Prevention or the Department of the United States Army.

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CHAPTER 2

Explosion Injuries Treated at Combat Support Hospitals in the Global War on Terrorism

Charles E. Wade, Amber E. Ritenour, Brian J. Eastridge, Lee Ann Young, Lorne H. Blackbourne, and John B. Holcomb

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INTRODUCTION

U.S. military combat support hospitals deployed in Iraq handle mass casualties on a regular basis. Over 65 percent of all wounded are the result of explosions. Among the initial survivors of these largely open space explosions, primary blast injury is very rare. More commonly diagnosed upon admission are secondary (penetrating), tertiary (crush), and quaternary (burn) injuries. Among the patient population at combat support hospitals, local civilians predominate, followed by U.S. active duty personnel and coalition soldiers. In accordance with the Geneva Conventions (FM) all receive the same expert standard of care. Outcomes, however, differ for different groups of patients. In particular, outcomes for young U.S. soldiers, who consistently wear body armor, contrast sharply to those of unprotected civilians of a wide range of ages with varying comorbidities.

Throughout this conflict, U.S. military personnel have maintained hospital records for all patients with traumatic injuries treated at combat support hospitals. The U.S. Army Institute of Surgical Research (USAISR) is responsible for the analysis of these data to evaluate the effectiveness of care delivered to military personnel. The USAISR mission is to provide requirement-driven combat casualty care medical solutions and products for injured soldiers; and to provide state-of-the-art trauma, burn, and critical care to Department of Defense beneficiaries around the world and to civilians in the USAISR trauma region. Many USAISR personnel have been deployed as surgeons, intensivists, and nurses in support of the Global War on Terrorism. Our group has undertaken a research effort to define the injury profile and improve the care of patients injured from explosions.

We have approximately 30,000 medical records available for study. Through the Joint Theater Trauma Registry (JTTR) that encompasses all medical events for all military services and care provided to civilians, USAISR researchers have entered and analyzed data for some 12,000 military patient records. Based on these data, studies of the effects of preventative measures and treatments on patient outcomes have led to significant changes in standards of care and improved results for soldiers. Examples of such improvements are the thoroughly revised guidelines for tourniquet use in the field and in emergency departments, improved hemostatic dressings now carried by every soldier, hypothermia prevention, new

algorithms delineating the use of fresh whole blood from "walking donors" in the absence of blood components, recommendations for improved staffing of intensive care units (ICU) with intensivists, and implementation of a theater-wide trauma systems approach for trauma care within the U.S. Central Command, including Iraq and Afghanistan. The scope of this chapter is to report the observed epidemiology of explosion injuries and to document some of the innovative care solutions crafted for the military population at combat support hospitals.

Mass Casualties, Explosions, and Collective Data

Mass casualty disasters are rare. But unfortunately, because of the scarcity of these events, apathy and complacency have prevented the initiation of comprehensive plans to deal with these disasters (Wightman & Gladish 2001). Existing plans are based upon single incidents or the compilation of information from a series of events. Meanwhile, bombing incidents are increasing worldwide (Champion, Mabee & Meredith 2006; Kapur et al. 2005).

Military physicians in the present precarious environment in Iraq and Afghanistan, who care for patients injured by explosions on a daily basis, have become familiar with these types of injuries. This familiarity often has prompted physicians to formulate and evaluate alternative approaches to patient care. The data they have collected in their efforts is a single source of information that far exceeds any other military or civilian database for this injury pattern. The U.S. military in Iraq can thus provide a nontraditional public health resource for the study of patients injured in explosions and the preparation of medical care facilities designed specifically to handle these events.

In the evaluation of disaster events associated with terrorism, emphasis usually is placed on chemical, biological, and nuclear events (Baker 2005; Bush et al. 2001; Jernigan et al. 2002; Karwa, Currie & Kvetan 2005; Okumura et al. 1996; Torok et al. 1997). However, most terrorism incidents involve the use of explosive devices and currently number in the thousands. In the U.S. State Department report on Global Terrorism, bombings accounted for 57% of events (U.S. Department of State 2005). To date, the number of lives lost, people injured, and impact on the existing trauma care infrastructure from explosions is far greater than all other mechanisms combined. Though clinicians

have more experience with injuries from explosions than those caused by chemical, biological, or nuclear events, data for demographics, care resource requirements, and outcomes usually are based on single incidents (Brismar & Bergenwald 1982; Cushman, Pachter & Beaton 2003; Gutierrez de Ceballos et al. 2005a, 2005b; Kirschenbaum et al. 2005; Lambert et al. 2003; Langworthy, Sabra & Gould 2004; Roccaforte 2001; Rodoplu et al. 2004, 2005; Teague 2004; Thompson et al. 2004; Wang et al. 2005; Zafar et al. 2005). Attempts have been made to collate data from multiple incidents; however, the resulting data sets have been limited to less than 1,600 patients (Kapur et al. 2005; Almogy et al. 2004; Almogy et al. 2005; Arnold et al. 2004; Arnold et al. 2003; Aschkenasy-Steuer et al. 2005; Ashkenazi, Olsha & Alfici 2005; Avidan et al. 2005; Einav et al. 2004; Karmy-Jones et al. 1994; Kluger, Kashuk & Mayo 2004; Kluger et al. 2004; Peleg & Aharonson-Daniel 2005; Peleg & Aharonson-Daniel et al. 2003; Peleg et al. 2004). Although these attempts have been valiant, the incidents reported usually have been isolated, affecting both data capture and experience of the providers. In contrast, in the present conflict in Iraq, military physicians are dealing with injuries from bombings on a daily basis. The military clinicians serving in the U.S. Military now have more than six years of continuous experience with tens of thousands of combat casualties, and arguably are the world's most experienced medical service. This iterative process has afforded them the opportunity to implement clinical guidelines for the care of these patients, and to institute a massive database to evaluate and study their efforts. For these reasons, and because of the unique data resources and expertise available to us, we have focused our research efforts on the acute care of military patients injured by explosions.

EXPLOSION CHARACTERISTICS

An explosion event (bombing) is defined by the FBI Bomb Data Center as "detonation of a device constructed with high or low order explosive material" such as dynamite; black, smokeless, and pyrotechnic material; or flash powder (Federal Bureau of Investigation 2007; Noji et al. 2005). More generally, the term "explosive" is used to describe energetic materials that react chemically to produce a detonation—a chemical reaction in which the reaction front advances into the unreacted material at or greater

than the sonic velocity of that material. The propagation of a chemical reaction in which the reaction front advances into the unreacted material rapidly, but at less than the sonic velocity of that material, is referred to as deflagration.

Explosives sometimes are classified in two categories, depending on their brisance or shattering effect. High brisance explosives are those that are effective at shattering casing materials and propelling fragments. Explosives that are effective at enhancing the overall blast effect on structures, but are not as effective at propelling fragments, are referred to as enhanced blast explosives.

When an explosive charge detonates in air the expanding gases push on the surrounding air, forcing out a shockwave—a sudden rise in pressure and other gas parameters to include temperature and density. The initial peak pressure and the peak shock pressure at any given distance from the detonation vary proportionally with the charge size. Currently there are methods the Department of Defense (DoD) researchers can use to accurately predict those pressures. These methods range from fast running DoD-developed empirical codes such as CONWEP, to longer running hydrocodes such as the Shock Hydrodynamic Automatic Mesh Refinement Code (SHAMRC), a code developed for the Defense Threat Reduction Agency.

Incendiary bombs are loaded with flammable materials such as propylene oxide and/or other ingredients such as chlorine trifluoride, white phosphorous, and reactive metal particles. They are intended to initiate fires to damage equipment and structures. Although incendiary bombs have been used in antipersonnel roles, for example, against enemy troop concentrations in open areas, their use against civilian personnel and/or targets in urban areas is prohibited by international conventions.

Although the overpressure created by an explosive can be highly destructive, it decays exponentially as a function of time and distance. For example, the peak overpressure from an artillery round at a range of 4 feet is 364 pounds per square inch (psi). At a range of 16 feet, the peak overpressure is only 17 psi (5% of the overpressure at 4 feet). For this reason, improvised explosive devices often are constructed to generate high-velocity fragments, or are loaded with metallic objects, which are propelled during the detonation. Whether from the breakup of the munitions casing, or from objects

embedded in the explosive, the objective is to increase the range and lethality of the explosive by generating secondary penetrating injuries. In addition to fragments, the lethality of an explosive sometimes is enhanced by the addition of chemical and flammable substances. The effectiveness of these additives varies widely, but there is some evidence that they can result in an increase in the number and severity of burn wounds.

EXPLOSION INJURIES

The cause of injury during an explosion is multifaceted (DePalma et al. 2005). When a device detonates, the resulting blast wave interacts with objects in its way. In the human body, the blast wave increases the pressure inside the body and produces stress and shear waves in body tissues. These waves are reinforced and reflected at tissue interfaces, thereby enhancing the injury potential, particularly in gas-filled organs such as the lungs, ears, and bowel. This is referred to as *primary blast injury*. In open spaces, few subjects within the area of the high pressure blast wave survive, as they are literally torn apart by multiple components (fragments, heat, toxic gases, dynamic pressure) of the blast environment. In closed spaces, such as inside buildings or in urban "canyons," primary blast injuries are more common, partially because the reflecting surfaces extend the duration and range of the blast wave, so that lethal overpressures can exist at further standoff distances or around corners, where the other components of the blast environment are basically benign. For example, blast lung injury is a major cause of immediate death at the scene of an explosion in closed space environments, but seldom the cause of death in initial survivors (Gutierrez de Ceballos et al. 2005a, 2005b; Avidan et al. 2005).

Following the shock front, the *blast wind*, which is the dynamic component of the blast wave, propels solid matter such as glass fragments and rocks, penetrating the patient. Penetrating injuries due to an explosion are termed *secondary injuries*, although they are often the primary cause of the injuries. The body may also be thrown into objects, resulting in blunt or crush injuries, referred to as *tertiary injuries*. The resultant heat, flames, and inhalation of hot gases and smoke from an explosion produce *quaternary injuries* such as burns.

In spite of the nomenclature characterizing blast injuries as primary, secondary, tertiary, or quaternary, victims of an explosion rarely suffer

from just one type of injury. The diverse etiology of injuries from explosions results in a complex and severe pattern of injury not encountered in any other situation. In open space explosions the injury patterns become more distinct as the casualty's initial position from the epicenter is increased.

The following statement in a National Research Council report sums up the availability of data on bombings:

> *Insufficiency of data on bombings. For technical evaluations, cost-benefit analyses, and formulation of a technically detailed rational response strategy, the data available today on illegal use of explosive materials in the United States do not constitute a suitable basis for a complete scientific analysis (National Research Council 1998).*

EXPLOSION STATISTICS

There are numerous government and private data sources with varying quantities of data. In the past year the Memorial Institute for the Prevention of Terrorism (MITP) (www.tkb.org) reported 2,449 terrorist bombings worldwide, representing 54% of the terrorist acts, in contrast to the year 2000 when there were 727 or 58% of all incidents. This represents nearly a 240% increase in bombings worldwide in the past five years. In the United States from 1980 to 1990, the FBI Bomb Data Center reported 12,216 bombings, an incidence of 1,222 per year (Federal Bureau of Investigation 2007; Noji et al. 2005). However, from 1991 through 1999, they reported 18,885 bombings, or an annual rate of 2,098, representing an increase of 72%. A recent review by Kapur summarized bombing incidents in the United States for the past 20 years (Kapur, Hutson et al. 2005). There were 36,110 bombing incidents. Of note, their data suggest a decrease in bombings in the United States from 1994 to 2002 of over 80%. In contrast, in Iraq the incidence of lethal bombings has more than doubled over the past 12 months, from an estimated incidence of 171 in 2004, to 350 in 2005 (O'Hanlon & Kamp 2007). Irrespective of the data source, the use of conventional explosive devices in terrorist acts are on the increase worldwide, are far and away the major device used by terrorists, and little data has been assimilated describing the optimal care of bombing casualties (Champion, Mabee & Meredith 2006). Thus, we

have a major public heath problem. For this reason information that can help to measure the impact on the health system and the care of injured patients following explosive events is paramount.

In 2005 the number of deaths from bombings worldwide was estimated to be 4,431. The vast majority of these deaths occurred in Iraq. In major bombings most deaths are immediate. The train bombings in Madrid in 2004 injured 1,885 people, of whom 177 (9.3%) died immediately and 14 (0.7%) after admission to hospitals (Gutierrez de Ceballos, Turegano-Fuentes et al. 2005a, 2005b; Frykberg 2005). In the London suicide bombings in 2005 there were approximately 700 who were injured; 56 (8%) people died immediately (Ryan and Montgomery 2005). In the Israeli database, bombing mortality after hospital admission was 6.1% with most deaths (56%) occurring within the first 24 hours (Kluger, Kashuk & Mayo 2004). In the United States for the years 1988 to 1997, bombs injured 4,490 people and killed 427 (9.5%). In the last year reported by the FBI Bomb Data Center (1999) there were 131 injuries with nine deaths (6.9%). In a 20-year period in the United States there were 5,931 injuries and 699 (10.5%) deaths from bombing incidents (Kapur et al. 2005). Arnold et al. reviewed 29 terrorist bombings that produced 8,364 injuries with 903 (10.8%) deaths (Arnold et al. 2004). In Iraq from the onset of the war in May 2003 to November 2005, data were collected for explosions in which there were more than three deaths during the incident (521); 14,653 civilians were injured (O'Hanlon & Kamp 2007). In these 521 incidents there was a total of 4,793 deaths (33%), amounting to nine per explosion. Although the mortality from bombs is initially devastating, the number of injured survivors and the complexity of their injuries pose the greatest challenge to the medical system.

Bombings result in a high incidence of wounded casualties. For 2005, MIPT reported 11,562 people injured in bombings, a rate of 4.7 people per bombing. The Brooking Institute reported 14,653 injured in Iraq, an average of about 28 per bombing (O'Hanlon & Kamp 2007). In the 2005 London bombings the injury rate was about 175 per bombing (Ryan & Montgomery 2005). Arnold et al. in a review of 44 mass casualty terrorist bombings found median hospital admission rates to range from 11 to 77% of those injured. This variance was a function of the type and strength of the bomb, and the environment where it was detonated

(Arnold et al. 2004; Arnold et al. 2003; Halpern et al. 2003). As with most disasters, bombings result in a large number of injured patients taxing the health care system. These patients often have multiple injuries. A review of 623 patients injured in explosions documented 1,170 injuries (Peleg et al. 2004). The major body regions injured were the extremities (arms and legs) followed by the head and face. In a subsequent review of an expanded data set from the same group, the majority of patients had more than one body region injured, with 11% having more than four regions injured (Kluger et al. 2004). In the Madrid bombings there were 243 patients with 691 injuries (Gutierrez de Ceballos et al. 2005a, 2005b). Of note, in 27 patients deemed critical there were 142 injuries. Of those patients admitted to ICUs after bombings, 86 to 100% had combined injuries (Shamir et al. 2005). The incidence of injuries to a variety of body regions and the combination of injuries (blast, penetrating, crush, and burn) make the care of victims of bombing a daunting task. For clinicians not used to caring for the multiplicity of injuries in one patient, much less 10 to 20, explosions create unique diagnostic difficulties.

UNIQUE INJURIES

Surgeons caring for victims of explosions must be prepared to handle complex and difficult wounding patterns not seen in normal practice. In addition they must be prepared to handle a greatly increased incidence of morbidity and mortality. These issues were well summarized in an editorial by Hirshberg (2004), who stated:

> *Terrorist bombings bring with them a host of new and vexing clinical problems. … What do you do with the hemodynamically stable, awake, and alert patient harboring dozens of small metal fragments in multiple body cavities, including the brain? How do you handle a "human remains shrapnel," a fragment of the suicide bomber's bone embedded in the chest of an asymptomatic patient? What if the suicide bomber is carrying a transmittable disease? Unexpected encounters with difficult clinical problems are the hallmark of MCIs (multiple casualty incidents). The answer must be learned from experience and rapidly disseminated to other surgeons facing the same challenges.*

The experience of U.S. military medical personnel in Iraq in the treatment of multiple injuries from numerous explosions provides another unique data source.

In the literature most information about the care and outcome of injuries from explosions has come from Israel where bombings occur once or twice a month. By comparison, combat support hospitals in Iraq are inundated with civilian causalities injured from explosives nearly every day. Treating casualties from explosions is a daily event. At combat support hospitals all nonmilitary patients receive the same care as U.S. military personnel. The combat support hospitals contain surgical subspecialists, intensive care unit capability, computed tomography scanning, and other advanced capabilities for stabilization and treatment of severely injured patients. Compared to trauma centers in the United States, combat support hospitals in Iraq are extremely busy caring for critically injured patients. For example, a single combat support hospital during a one-year period admitted 3,444 trauma surgical cases, of which 90% had penetrating injuries. Among these cases, 703 (20%) required blood transfusions, of which 164 (4.8%) needed massive transfusions (≥10 units). This is in contrast to a major trauma center (University of Maryland Shock Trauma Center) that saw 5,649 injured patients in a year with 20% penetrating injuries, 452 (8%) patients requiring transfusion, and 143 (2.3%) needing massive transfusions (Como et al. 2004).

Improvements in the care of the critically injured soldier in the field have altered the demographic of military fatalities. The present conflict has seen a reduction in the rate of soldiers killed in action (KIA) and in the case fatality rate (CFR) compared to Vietnam and World War II (WW II) (see Table 2-1) (Holcomb et al. 2006). However, the rate of soldiers who died of wounds (DOW; death in a medical facility) has increased, suggesting that a more severely injured group of patients is admitted to the hospital. In both World War II and Vietnam, of the soldiers who died, 88% were classified as KIA and 12% DOW. Because of the significant reduction in the KIA rate in the current war, a greater percentage of patients are dying after reaching a military medical treatment facility. In the present conflict, 23% are classified as DOW and 77% KIA. Though the CFR has decreased, the near doubling of the rate of those dying after admission to a military treatment facility emphasizes the need to focus resources and research to aid these casualties.

Table 2-1 Comparison of Proportional Statistics for Battle Casualties for U.S. Military Ground Troops from WW II, Vietnam, Afghanistan/Iraq (Holcomb et al. 2006)

	WW II (Almogy et al. 2004; Amir et al. 2005)	Vietnam (U.S. Department of State 2004)	Total Iraq/ Afghanistan (Gennarelli & Wodzin 2005; R.I. Committee on Marking, and Licensing of Explosive Materials 1998)
KIA (%)	25.3[a]	18.6[b]	12.5[c]
DOW (%)	3.5[a]	3.0[b]	4.1[c]
CFR (%)	19.1[a]	16.1[b]	8.8[c]

a>b>c, p <0.01.

DEMOGRAPHICS OF EXPLOSIONS IN MILITARY PATIENTS

The combination of anatomical information, as to the extent of injury, coupled with physiological data greatly improves the understanding of a mode of injury. Patients injured in explosions challenge standard civilian trauma models and scoring systems as their injuries are located in multiple body regions. As noted earlier, victims of explosions present with primary, secondary, tertiary, and quaternary injuries. Further, as the complexity and number of injuries increase so does mortality and morbidity, such as increased contamination and subsequent infection (Santaniello, Luchette et al. 2004). Kluger et al. referred to victims of explosions as a new class of trauma casualties, much different from those created by conventional trauma (Kluger, Kashuk & Mayo 2004; Kluger et al. 2004; Santaniello et al. 2004). Knowledge as to epidemiology of patients with injuries from explosions is essential in determining medical requirements to impact outcomes.

As of mid-2007 there were 3,300 U.S. military personnel killed and 24,300 wounded as a result of Operation Enduring Freedom and Operation Iraqi Freedom. Of those injured, 66 to 72% were the result of explosions. Of interest is that these rates of injury from explosions are similar to those observed in World War II (64%) and in Vietnam (63%). The rate of injury by explosions has been consistent when individual injury types have been investigated. In burn patients Wolf et al. (2006) reported injury due to explosions to be 52% of the population, whereas for extremity injuries Owens et al. observed a rate of 79% (Owens et al. 2008).

The means of causing explosion injuries is diffuse. Owens et al. (2008), in a review of 1,566 patients with combat extremity injuries, reported 79% were the result of explosions, of which the majority were the result of improvised explosive devices (IEDs) (see Table 2-2). In an evaluation of all injury types the overall rate from explosions was 77%, with 71% of these from IEDs. In another recent report of hostile injuries from explosions, as much as 88% were from IEDs. We have combined patients injured by IEDs, rocket-propelled grenades, or mortars using the broad term explosion as the method of injury. This compilation is done in that the clinical presentation is similar for all means of explosive injury.

INJURIES

Primary Injury

The number of primary blast injuries from explosions that present to military medical care facilities is limited. Primary blast injuries rarely are noted upon autopsy in those patients that die on the scene, and they are extremely rare in those patients admitted to the hospital and subsequently die. In a recent study, Ritenour et al. (2007) reviewed the occurrence of primary blast injury in patients with burns (n = 333) or amputations (n = 97) from explosions. The incidence of tympanic membrane rupture, diagnosed upon admission by an otolaryngologist, was 21% for burns and 6% for patients, with amputations rates similar to those reported by others (Katz, Ofek et al. 1989). Eight patients (1.9%) had blast lung injuries and only one (0.2%) had a primary blast injury to the intestine. All these patients had burn injuries. Thus, for the total population (n = 430) the incident rate of life-threatening primary blast

Table 2-2 Mechanism of Explosion Injury of Military Casualties (NR: not recorded)

	Owens et al. 2008 (n = 1,146)	JTTR (n = 4,365)	DIOR (n = 19,092)
IED	49%	71%	88%
Landmine	4%	11%	(NR)
Mortar	24%	3%	11%
Bomb	3%	(NR)	(NR)
Grenade	20%	15%	0.3%

injury was 2%. Previous civilian data on all admissions with injuries from explosions suggest a rate on the order of 0.1 to 0.2% (Avidan et al. 2005; Hadden et al. 1978).

The higher incidence in the present study is related to the severity of injury of the patients, since those with primary blast injuries were all burned, suggesting they were in close proximity to the explosion and thus represent a selective population in contrast to all patients admitted to the emergency department. In civilian patients injured in explosions, burns greater than 10% of the total body surface area were associated with blast lung injury 7.5% of the time (Almogy et al. 2005). The lower rate of primary injury observed in military casualties with burns (2.5%) may be related to the fact that most of the explosions experienced by military personnel are in open spaces (Arnold et al. 2004). Additionally, military personnel typically are wearing protective gear; in a recent study by the Department of Defense's Technical Support Working Group using porcine models, those subjects wearing ballistic protective gear *including* hard armor received substantially reduced primary blast lung injuries (Walilko & Young 2006).

In the study by Ritenour et al. (2007), of the eight patients who had blast lung, only two had tympanic membrane rupture. In agreement with an earlier study, lack of eardrum perforation in patients injured in an explosion does not appear to be a marker of absence of blast lung injury (Almogy et al. 2005; Leibovici, Gofrit & Shapira 1999). Therefore, as a screening tool, absence of tympanic membrane rupture should not be used to rule out blast lung injury.

Secondary Injury

The dominant injuries in military explosion casualties are penetrating injuries. This is similar to the civilian data (Gutierrez de Ceballos et al. 2005a, 2005b; Rodoplu et al. 2004, 2005). Most of the civilians are seen in the hospital but are not admitted (Armand & Hess 2003). For example, in the Madrid bombings only 28% were admitted (Gutierrez de Ceballos et al. 2005). In the civilian experience, of those patients admitted to the hospital the incidence of penetrating injuries is 65 to 90% (Gutierrez de Ceballos et al. 2005a, 2005b; Rodoplu et al. 2004). In the military databases, when injury type is classified it is based upon the predominant injury requiring medical intervention after admission. Thus, there is only

one injury type per patient. In a review of 4,635 patients we found 56% to have predominantly penetrating injuries. Owens et al. (2007), in a study of extremity injuries from explosions, noted 53% of injuries were penetrating. Chambers and colleagues noted a penetrating injury rate of 62% (Chambers et al. 2006). Penetrating injuries are the predominant injury type seen in the emergency department in military patients; with admission the rate is on the order of 50 to 60%. Penetrating injured patients most often require operative care that is extremely different from blunt injured civilian casualties who rarely require emergent operative intervention. These differences in mechanism and care will cause a significant burden on the unsuspecting civilian trauma system.

Tertiary Injuries

In the present conflict the incidence of tertiary blast injury (blunt/crush) is far below that reported in civilian trauma. This difference is likely related to the majority of military explosions occurring in open rather than closed spaces, such as buildings where there is a high incidence of structural collapse (Arnold et al. 2004). The blunt injury incidence in our review of military casualties was 36%.

Quaternary Injuries

Burns comprise 8 to 10% of casualties sustained in conflicts since World War II (Cancio et al. 2005; Shafir et al. 1984; Sidel'nikov, Paramonov & Tatarin 2002). The incidence varies based on the predominant type of weapon. Burns comprise 5% of casualties evacuated from conflicts in southwest Asia. Many of these burns result from the enemy's detonation of explosives. Wolf et al. (2006) reviewed the records of burn patients treated at USAISR between April 2003 and May 2005 to evaluate mission impact and provide recommendations for improved combat burn protection.

Records were obtained and data for demographics, burn severity and pattern, and early outcomes were collected for 274 military burn patients. One hundred forty-two (52%) sustained burns in explosions from hostile action. Age was 26 ± 7 years (mean ± SD). Mortality was 4%. The annual rate of explosions as a cause of burns increased from 18 to 69% during the two-year period. Total body surface area burned increased from 15% ± 12 to 21% ± 23, Injury Severity Score (ISS) rose from 8 ± 11 to 17 ± 18, and frequency of inhalation injury rose from

5 to 26%. The hands (80% of patients) and the face (77%) were the most frequently burned body areas. Burns were isolated to the hands in 6% of patients and to the face and hands in 15%. An average of 52% ± 30 of the surface area of the hands and 45% ± 26 of the face was burned. Mean length of stay was 24 ± 25 days (median, 14). Though 77% of patients were discharged without global disability, only 36% returned to their previous duties. A similar pattern of injury and disposition was seen at the Army burn center during the war in Vietnam (1966–1968), but mortality was higher (7.9%) (Allen, Whitson & Henjyoji 1970).

In summary, from the onset of the present conflict, burns resulting from combat explosions have increased in frequency, size, and injury severity. Burns are concentrated on areas not protected by clothing. These injuries create long hospital stays and frequently prevent patients from returning to their previous work.

ANATOMICAL DISTRIBUTION OF INJURIES

Anatomical location of explosive injuries is widely distributed about the body (Thompson et al. 2004). Of note, the distribution of injuries is related to the body area exposed. Kauvar et al. (2006) demonstrated that the location of burns was related to the percentage of the body at risk in combat casualties. Owens et al. (2008) reiterated this finding in Table 2-3. In an evaluation of 1,566 military personnel with 6,609 wounds from combat they noted that there was a decreased incidence in thorax injuries proportional to total body surface area. However, it should be remembered that this area is at reduced risk of injury due to personnel protective equipment. The average number of injuries per patient was four. These findings reaffirm the global involvement of body regions from explosive injuries.

Table 2-3 Distribution of Wounds by Body Region (Owens et al. 2008)

	% of Body Surface Area	% Wounds per Body Area
Head/Neck	12	30
Thorax	16	6
Abdomen	11	9
Extremities	61	55

Injury of soft tissue is the most common type of extremity wound (53%), followed by fractures (26%). Most fractures are of extremity long bones, and are often open (82%). In a review of battlefield injuries we found the fractures to account for 36% of injuries, and open wounds, 36%. The preponderance of soft tissue injury and open fractures raises a wide range of issues as to infections that is not dealt with in this review (Murray et al. 2006).

AGE

Age is an important determinant of outcome in patients with traumatic injuries. Older and younger patients with traumatic injuries have a lowered probability of survival compared to those between the ages of 18 and 55 years with equivalent injuries (Baker et al. 1974; Baker & O'Neill 1976; Garcia & Brown 2003; MacKenzie et al. 2006; MacLeod et al. 2004; Moreau et al. 2005; Nagappan & Parkin 2003; Napolitano et al. 2001; Nirula & Gentilello 2004; Victorino et al. 2003). This is emphasized in a recent report by MacKenzie et al. (2006). Hospital mortality for patients treated at a trauma center was 12.3% for those over the age of 55 years compared to 5.9% for younger patients. Seventy-nine percent of military casualties seen at combat support hospitals range between 18 to 30 years of age. For injuries due to explosions, the Israel Trauma Group found 7.3% of the population to be under 15 years of age and 8.7% to be over 59 years old (Peleg et al. 2003, 2004).

There have been limited studies as to the effect of age on outcomes in patients with injuries from explosions. A review of children injured in the Oklahoma City bombing found the primary cause of death (90%) to be head injury (skull fractures) (Quintana et al. 1997). In light of a child's small mass, increased tertiary injury would be expected. Of the 47 children sustaining nonfatal injuries, only seven required hospitalization. Four of these were also due to head injuries. In reviews of bombing incidents in Israel, injury of children in explosions was contrasted with other forms of trauma suffered by children (Aharonson-Daniel et al. 2003; Amir et al. 2005). However, the profiles were not contrasted with adult victims. Of the 158 children injured, 34% required ICU stays in comparison with a 23% rate in all patients (Peleg et al. 2003, 2004). Further, the incidence of ISS >25 was 25% in children and 16% in all patients. These findings were supported in

a subsequent review (Waisman et al. 2003). In a military hospital in Afghanistan, of 90 patients that required surgery, 22% were under the age of 19 (Beekley & Watts 2004). In an evaluation of a limited population from one combat support hospital in Iraq there were 709 patients among 967 with age recorded, of which 3% were over the age of 55 years (McGuigan et al. 2007). Eleven percent were children (age <18 years). In 39% of children, explosion was the cause of injury. The mortality rate among children was 9.5% in contrast to 3.8% in adults ($p < 0.01$). McGuigan et al. recently reported a mortality rate of 7% in 99 pediatric patients (mean age, 10 years) treated in a combat support hospital (McGuigan et al. 2007). We presently do not have information on the extent of injury to adjust comparisons between age groups but would hypothesize that patients with injuries due to explosions under the age of 18 years and over age of 55 years have poorer outcomes compared to patients between 18 and 55 years of age. In evaluation of data from military patients injured by explosions, age should be considered as the age range of military patients, 18 to 35 years, is optimum for a positive outcome.

GENDER

Gender has been suggested as a factor in the outcome of victims of traumatic injury (Choudhry et al. 2005). In civilian explosions the proportion of females injured is about 40% (Brismar & Bergenwald 1982; Peleg et al. 2003), whereas in military casualties, as expected, the majority of injured are males (98%). However, the rate of death is similar at 11% for males and 13% for females. Gender does not appear to impart a survival advantage to military casualties of explosions.

INJURY SEVERITY

Injury severity scores are used to direct care and evaluate potential outcome (disabilities and mortality) (Baker & O'Neill 1976; Baker et al. 1974; Boyd, Tolson & Copes 1987; Champion et al. 1989, 1990; Shoemaker et al. 2001, 2005). The most commonly used tools are the Abbreviated Injury Scale (AIS) and ISS, which have been related to threat to life, mortality, need for hospitalization, ICU days, overall length of stay, treatment cost, disability, and quality of life (Baker 2005; Baker et al. 1974; Baker

& O'Neill 1976). In studies among trauma centers, the AIS has been used to define patient populations for comparative purposes. Kluger et al. (2004) reviewed the relationship of injury pattern from explosions to outcomes in 906 patients. The mortality rate was 5.7%, and 28% had an ISS of >15. Based on ISS, in comparison with other forms of trauma, injuries from explosions did not increase mortality or length of stay (LOS) in the ICU. However, for a given ISS, patients injured in explosions had a longer hospital LOS.

Peleg et al. contrasted outcomes of patients with injuries from explosions (n = 623) with those from gunshots (n = 419). A similar percentage of patients with gunshot wounds (25%) and patients injured by explosions (26.4%) had an ISS >15. However, a greater percentage of the patients with injuries from explosions were admitted to the ICU and had hospital stays longer than 14 days. Chambers and coworkers (2006) compared outcomes of a military surgical unit to those of a major urban hospital for patients stratified by ISS. For patients with severe (ISS 16–24) and very severe injuries (ISS >24) there was no difference in mortality between centers. However, all the urban patients had gunshot wounds in contrast to the military population, where the majority were injured by explosive devices.

Recently, the AIS was revised to account for injury characteristics specific to military conflicts (Gennarelli & Wodzin 2005). This revision was made to reflect the increased threat to life or increased impairments due to bilateral injuries. In addition, increased emphasis has been given to organ and fracture classifications. The ISS is an integral part of trauma registry severity of injury assessment. The ISS is calculated from the highest AIS codes for three body regions. Each AIS (a scale of 0–6) is squared and the values summed to attain the ISS. If a single region has an AIS of 6 (currently untreatable), an ISS of 75 is assigned, indicative of an expectant outcome. For 3,004 patients injured by explosions we compared the military AIS with the 1998 standard AIS versions by calculating ISS. There was an increase in ISS from the 1998 AIS version in 18% of the patients. In the 1998 versions, 0.3% of the patients were given an ISS of 75, in contrast to the military version where the rate was 3%. Of the overall population 5% of patients died. We suggest that the military version of AIS is a better indicator of outcomes for patients injured by explosions than other versions of AIS.

Employing the military scoring system will adjust ISS and allows appropriate comparisons between different modes of injury and prediction of outcome.

PROCEDURES

In critically ill patients the type and number of procedures performed impacts outcome and medical resource utilization. Following the Madrid bombings in 2004 there were 29 patients deemed in critical condition, with two of these dying within minutes of arrival at the hospital. In the first 24 hours after the incident there were 37 urgent or emergency surgical procedures performed on 34 patients. The primary surgical interventions performed were orthopedic (41%). Use of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes and procedure categories allows the impact on resources and outcome to be evaluated. For example, an injury profile requiring life-saving interventions may be identified. In combat support hospitals the majority of the operative procedures (20,517) were on the musculoskeletal system (21.5%), integumentary system (22.6%), and cardiovascular system (10.2%). Another 26.1% were diagnostic and therapeutic procedures. Irrigation and debridement is the most common procedure as reported by others (Chambers et al. 2005, 2006). For the integumentary system, 74% of the procedures were for wound debridement in contrast to the musculoskeletal system, where 32% of the procedures were for debridement of open fractures of long bones of the extremities. Outcome and resource utilization for these procedures are dramatically different. Patients with explosion injuries require increased medical resources due to multiple injuries, necessitating an increased number of complex procedures and longer lengths of stay in the ICU and hospital.

HEMOSTATIC RESUSCITATION

The primary cause of death on the battlefield is blood loss (Bellamy 1984). In the civilian population about 40% of deaths from traumatic injuries are due to exsanguination (Sauaia et al. 1995). Coagulopathy is a major contributor to bleeding-related morbidity and mortality in patients with traumatic injuries (Carr 2004; Cosgriff et al. 1997; Hoffman 2004; Hoyt et al. 1994; Lynn et al. 2002). Of note is the work of Brohi et al. (2003)

that evaluated mortality in coagulopathic patients and that showed the effect of coagulopathy on mortality independent of the ISS. In the critically injured patient (ISS >15), the presence of coagulopathy upon admission significantly increased mortality, indicating an independent effect on survival. Diagnosis and treatment of coagulopathy in victims of trauma, especially those of explosions with multiple penetrating injuries, is vital to a positive outcome.

It is interesting to note the lack of information on the use of blood products, or the presence of coagulopathy upon admission in patients injured in explosions. Among the survivors of explosions, hypotension associated with bleeding is common. Upon admission to the emergency room, 6% of patients injured in explosions have a systolic blood pressure <90 mmHg, in contrast to 2.5% for other types of trauma (Shamir et al. 2005). However, there are no studies that specifically define fluid and blood requirements of bombing victims. As over 86% of patients admitted to the emergency room have combined injuries, we expect there would be significant requirements for blood products. A single combat support hospital in which the majority of injuries were from explosions during a one-year period had 703 patients (21% of the patients) who required blood transfusions in contrast to a major U.S. trauma center that had 452 (8% of patients) patients requiring transfusion (Como et al. 2004). In addition, there was a greater incidence of patients requiring massive transfusions (>10 units of blood products). Patients who require massive transfusions use a large number of hospital resources, have a high rate of morbidity, and poor outcomes (Como et al. 2004; Armand & Hess 2003; Cosgriff et al. 1997; Brohi et al. 2003; MacLeod et al. 2003; Malone et al. 2003; Shafi & Kauder 2004). Patients requiring massive transfusions represent about 20% of the patients transfused, yet they consume 80% of the resource.

In the combat support hospital there were 9,537 units of blood products transfused, of which 80% was used for patients requiring massive transfusions. The amount of blood transfused is closely correlated with the incidence of medical complications and multiple organ dysfunction (MOD), as well as mortality rates (Malone et al. 2003). Upon admission to the combat support hospital, the INR, an indicator of coagulation status in patients requiring massive transfusion, was 2.5 ± 1.5 (mean ± SD) in contrast to normal levels of less than 1.5. The increase in INR is indicative

of coagulopathy upon admission (Schreiber et al., in press). In patients whose outcome was known, 15% had MOD and the mortality rate was 48%. These rates are greater than those observed in the general population. In a preliminary analysis of 159 patients from one combat support hospital, the mortality was 30% if INR was elevated >1.5, in contrast to 5% for patients with a normal level.

Massive transfusion patients often present with hypothermia, acidosis, and coagulopathy, a condition that takes 30 to 60 minutes to diagnosis. In addition, the present treatment regime often initiates administration of packed red blood cells prior to the receipt of lab values, which further dilutes coagulation factors and aggravates bleeding (Hess & Thomas 2003). Early diagnosis of patients who require massive transfusions will aid in having the right products available, and offer the opportunity to initiate alternative therapies such as administration of immediate use of thawed fresh frozen plasma (Borgmann et al., in press; Holcomb et al. 2007).

CLINICAL LESSONS LEARNED

Although the physics of primary blast injury is interesting, by far the most lethal effects of commonly used explosives are their ability to produce massive penetrating and blunt trauma. Such horrific injuries rarely are seen in the civilian trauma setting. Explosions may simultaneously cause traumatic amputations to multiple extremities and penetrating or blunt trauma to the torso and/or head, and burns. The U.S. military has seen an increase in the frequency and severity of explosion injuries over the course of Operation Enduring Freedom and Operation Iraqi Freedom and therefore has gained much experience in treating these injuries. Exsanguination is the most common cause of death on the modern battlefield and in victims of explosions.

The complexity and magnitude of explosion injuries in a single patient presents the physician with both diagnostic and therapeutic challenges. Patients with traumatic amputations may have suffered significant but not quantifiable blood loss in the field prior to placement of a tourniquet and may arrive at a hospital in extremis. The physician is then confronted with the challenge of treating hemorrhagic shock while diagnosing the source of ongoing hemorrhage in a patient with hundreds of holes.

Physical examination alone may be unhelpful for two reasons. First, numerous, diffuse, small wounds may make prioritization of injuries difficult. This diagnostic and therapeutic dilemma can be addressed, in part, by use of CT, when clinically possible. Second, a large gaping wound with associated major vascular trauma may seem to account for a patient's shock but may not be the only injury requiring immediate surgical intervention. The surgeon should bear in mind that the obvious injury may not be the immediately lethal one and should have a high clinical suspicion for ongoing occult hemorrhage in any victim of explosion. The lack of visible wounds to a particular body region should not be considered an indication that no or only minimal injury is present. Explosions may produce small fragments that leave unimpressive cutaneous lesions but may penetrate the great vessels or heart. Additionally, blunt or tertiary-type blast injuries may produce severe lacerations of the heart, lungs, and abdominal viscera or vasculature, yet leave little if any external sign of trauma.

A reasonable approach to this type of patient may be to gain definitive control of the obvious hemorrhage and then continue resuscitation while performing a planned diagnostic pause in the operating room. The few minutes taken to perform a quick evaluation of the chest with X-ray and heart and abdomen with ultrasound may reduce the chances of death due to undiagnosed, hidden hemorrhage during definitive repair of other injuries. Principles of damage control resuscitation and aggressive surgery should be utilized. If the possibility of occult hemorrhage in the chest, abdomen, or extremities has been ruled out, progressive cerebral edema or intracranial hemorrhage may account for clinical decompensation. Damage control surgery techniques are widely practiced, decreasing the time spent in the operating room, and making room for the next patient.

In summary, patients injured in explosions may have both readily apparent and hidden wounds that are equally lethal if left untreated. Physicians should have a high clinical suspicion for occult hemorrhage or closed head injury. After control of the immediately life-threatening injuries in the operating room, it may be advisable to perform rapid diagnostic imaging to evaluate for occult hemorrhage before committing to a definitive operation. By the time a patient is determined to be unresponsive to resuscitation, the window of opportunity for life-saving intervention may have passed. Finally, all explosion-injured patients should undergo otoscopic

examination prior to discharge to assess for tympanic membrane rupture and allow for appropriate treatment and continuing care.

SUMMARY

Most military patients seen in combat support hospitals have injuries due to explosions. The incidence of primary blast injury is minimal, as the majority of patients have penetrating and/or blunt injuries. Burns account for about 3 to 5% of injuries. Multiple injuries are the norm. The area of the body injured is proportional to the percent of the body surface area at risk. The primary cause of potentially preventable death both before and after admission is hemorrhage. These findings are similar to those seen in previous conflicts and in the civilian population. The majority of patients who die of wounds bleed to death, thus aggressive correction of coagulopathy and control of bleeding is warranted. Victims of explosive injuries have extended stays in intensive care and hospital as the magnitude and diversity of their injuries is greater than those from gun shots or shrapnel alone.

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PART 2

Pathology and Pathophysiology of Blast Injuries

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CHAPTER 3

Pathology of Human Blast Lung Injury

Michael Tsokos

CHAPTER CONTENTS

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Injuries Caused by Explosives—A Short Overview
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    Thermal Injuries
Pathological Features of Traumatic Lung Injury not due to Primary Blast Effects
Blast Lung Injury
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Concluding Remarks

INTRODUCTION

Due to the increasing number of armed conflicts and the continuous rise of urban terrorism worldwide, death and injury from explosives are becoming ever more frequent. Blast lung injury occurs in both combat and civilian bombings and is one of the most devastating threats facing victims of explosions (Mellor & Cooper 1989; Mellor 1992; Leibovici et al. 1996; Mayorga 1997; Pizov et al. 1999; Tsokos et al. 2003a, 2003b; Aggrawal & Tsokos 2005). However, few, if any, clinical pathologists have great experience with the pathological features of blast lung injury since the

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investigation of deaths caused by explosives is a domain of forensic pathologists. Death from explosives is always a nonnatural mode of death and therefore, forensic pathologists are frequently involved in the determination of manner (homicide, suicide, or accident) and cause of death as well as in the identification of those who have died from explosions.

After a short overview of the different types of injuries victims of explosions may sustain, this chapter provides an overview of our present-day knowledge on the pathological features of human lung injury following explosions, with special emphasis devoted to the pathology of human blast lung injury. Human blast lung injury represents an exceptional and unique pattern of lung pathology not comparable to any other spectrum of natural or nonnatural lung disease encountered by both clinicians and pathologists.

INJURIES CAUSED BY EXPLOSIVES—A SHORT OVERVIEW

The detonation of a chemical (volatile or solid) explosive leads to a rapid expansion of gas, which, upon release of its potential energy, creates a shock wave. This radially propagating, large-amplitude overpressure wave transmitted into the surrounding environment after an explosion is known as the *blast wave*.

Victims of explosions usually suffer from a combination of blast lung injury, blunt force trauma, penetrating injuries, and burns. The type, distribution, and severity of injuries of bombing victims most often indicate their location in relation to the epicenter of explosion (Katz et al. 1989; Hiss & Kahana 1998; Tsokos et al. 2003b). Explosions set off in confined spaces (e.g., mines, buildings, or large vehicles) are associated with greater morbidity and mortality than explosions set off in the open air because of multiple reflections of the blast wave off walls and other obstacles and due to the possibility of structural collapse of buildings where the detonation took place (Cooper et al. 1983; Mellor 1992; Leibovici et al. 1996).

According to the underlying physical mechanisms, injuries caused by explosives can be classified into two broad categories: *blast injuries* and *thermal injuries*, as well as their respective subcategories *primary, secondary, tertiary,* and *quarternary blast injuries,* and *primary* and *secondary thermal injuries* (Table 3-1).

Table 3-1 Classification of Injuries Caused by Explosives

Category	Underlying Physical Mechanism	Type of Injury
Blast Injury		
Primary blast injuries	(Direct) blast wave exposure	Rupture of gas-containing organs (e.g., lungs, middle ear, gastrointestinal tract), perforation of hollow organs. Also, depending on the distance between place of detonation and the affected body, disruption of the body, traumatic amputation of limbs, gaping lacerations of the skin and the internal organs
Secondary blast injuries	Blast-energized bomb fragments and other debris (shrapnel)	"Missile injuries": bruises, puncture abrasions, puncture lacerations, penetrating trauma
Tertiary blast injuries	Abrupt deceleration of the body on rigid objects following acceleration due to (indirect) blast wave effect	Blunt force trauma, penetrating trauma
Quarternary blast injuries	Collapse of a building or falling down of parts of a building	Miscellaneous; mostly blunt force trauma (e.g., crush injuries from falling masonry) but also penetrating trauma
Thermal Injury		
Primary thermal injuries	(Direct) flash burns resulting from the blast wind	Burns, singeing of head hair and eyebrows. Flash burns are usually affecting exposed (undressed) areas of the body. These primary thermal injuries are generally more superficial than those seen as a result of secondary thermal injury
Secondary thermal injury	(Indirect) burns from material ignited, burns from local ignition of clothing	Severe burns, usually rendering identification difficult or impossible

Blast Injuries

Primary Blast Injuries

Injuries directly inflicted on the human body by a blast wave are referred to as primary blast injuries. When individuals are located in the immediate vicinity of an explosive at the time of detonation, gaping lacerations of the skin and the internal organs and severe mangling of body parts may occur, or the victims' bodies may be even totally disrupted (Hiss & Kahana 1998; Tsokos et al. 2003a, 2003b; Crane 2005).

Traumatic amputation of limbs is a frequent finding, especially in those who were located in the immediate vicinity of the explosive at the time of detonation (Aggrawal & Tsokos 2005; Hiss & Kahana 1998; Tsokos et al. 2003a; Shields et al. 2003; Crane 2005). As a direct effect of the blast wave that creates powerful shearing forces that act in a coaxial direction relative to the bone, comminuted fractures of long bone shafts may result. Limb flailing caused by the blast wave then completes the amputation by disrupting the soft tissue (Hull & Cooper 1996).

Apart from whole body disruption and amputation of limbs, direct blast wave exposure almost exclusively affects gas-containing organs. Due to complex phenomenons taking place between the blast wave and objects in its path such as the occurrence of marked pressure stresses at air/fluid interfaces, gas-containing organs such as the lungs, middle ear, and gastrointestinal tract are the organs most vulnerable to overpressure brought about by the blast wave. The resulting pathological findings are blast lung injury, tympanic membrane rupture, and bowel contusion and/or bowel perforation in the absence of penetrating abdominal wall wounds (Phillips 1986; Mayorga 1997). Primary blast injuries are estimated to contribute to 47 to 57% of injuries in survivors and to 86% of fatal injuries (Mayorga 1997).

Secondary Blast Injuries

Secondary blast injuries result from blast-energized bomb fragments and other displaced objects at the site of explosion such as fragments of glass, casing, and masonry, causing penetrating trauma (Cooper et al. 1983; Leibovici et al. 1996; Tsokos et al. 2003b; Shields et al. 2003; Aggrawal & Tsokos 2005). The characteristic type of injury due to blast-energized bomb fragments and displaced debris from the scene of explosion is a combination of bruises, puncture abrasions, puncture lacerations, and

penetrating wounds (Hiss & Kahana 1998; Crane 2005); this type of injury is referred to as *missile injuries*, *propeller injuries*, or *peppering injuries*.

Tertiary Blast Injuries

Tertiary blast injuries occur when the body is accelerated from the blast wave at first and is then abruptly decelerated on rigid objects, thus resulting in mainly all types of blunt force trauma and, occasionally, in penetrating trauma (Cooper et al. 1983; Leibovici et al. 1996; Shields et al. 2003).

Quarternary Blast Injuries

Quarternary blast injuries are defined as those injuries of victims of explosions that are due to the collapse of a building or falling down of parts of a building where the explosion took place (Aggrawal and Tsokos 2005). This type of injury is mostly blunt force trauma such as crush injuries but penetrating trauma and asphyxia of those who are buried under the debris is also frequently observed.

Thermal Injuries

Significant skin burns may be inflicted by explosions. The severity of a burn is directly related to the temperature rise within the skin and the duration of this rise. One has to differentiate between primary and secondary thermal injuries (see Table 3-1).

Primary Thermal Injuries

Although the term *blast wave* refers to the intense over-pressurization impulse created by a detonating explosive, this phenomenon has to be distinguished from the term *blast wind*, a forced super-heated air flow (heat radiation) that is generated by the explosion. It is characteristic of bombings that flash burns inflicted by the blast wind (so-called primary thermal injuries) are usually limited to exposed (undressed) areas of the victim's body since clothing usually provides good protection from flash burns (Rajs, Moberg & Olsson 1987; Mellor 1992; Tsokos et al. 2003b). These primary thermal injuries are generally more superficial than those seen as a result of secondary thermal injury (see next).

Secondary Thermal Injuries

Burns occupying large surface areas and affecting those body areas covered by clothing prior to the explosion imply that either the heat was of such

intensity that the victim's clothing caught fire or that the location where the detonation took place caught fire (Aggrawal & Tsokos 2005). These burns are designated as secondary thermal injuries and are usually more severe than primary thermal injuries.

PATHOLOGICAL FEATURES OF TRAUMATIC LUNG INJURY NOT DUE TO PRIMARY BLAST EFFECTS

In victims of explosions, a wide range of traumatic lung injuries may lead to instant death or to progressive respiratory failure with potential fatal outcome. Not all lung injuries following an explosion are due to the effects of the blast wave. Besides blast lung injury, a number of different physical mechanisms taking place during and very shortly after an explosion can lead to considerable lung injury.

Following an explosion, blast-energized bomb fragments or debris can lead to penetrating or nonpenetrating impacts to the thorax. The lungs may sustain contusions and bruises by direct blows to the chest by bomb fragments, debris, or fallen masonry. Lung contusions may also result from blunt chest trauma due to the victim's body by being thrown against solid surfaces/rigid objects as a result of displacement by the blast wave-induced mass movement of air. In addition, hematothorax and pneumothorax may result from penetrating or nonpenetrating impact trauma of the chest wall. Fractures of bones of the thoracic cage and their missile-like traumatizing effects as secondary projectiles (see Figure 3-1) can lead to a life-threatening condition or even death of the victim.

When a projectile passes through the body, two different mechanisms of wound formation must be differentiated: (1) primary tissue damage due to crushing and shredding of tissue in the direct path of the projectile (missile track), and (2) radial acceleration and flinging outward of tissue adjacent to the missile track, producing the temporary cavity. The temporary cavity undulates for 5 to 10 ms before it becomes to rest as the permanent cavity. The size of the temporary cavity is determined by the amount of kinetic energy absorbed in the tissue, which is again influenced by the velocity of the discharged projectile or projectile-like material, and the density and cohesiveness of the affected tissue. The combination of both direct tissue destruction in the path of the projectile and temporary cavity formation determines the final extent of a missile wound (DiMaio 1999).

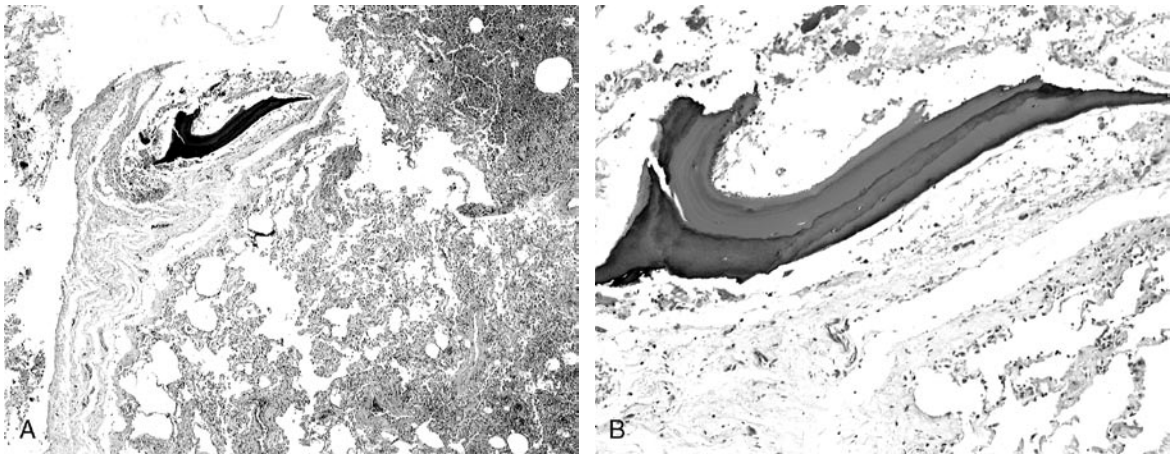
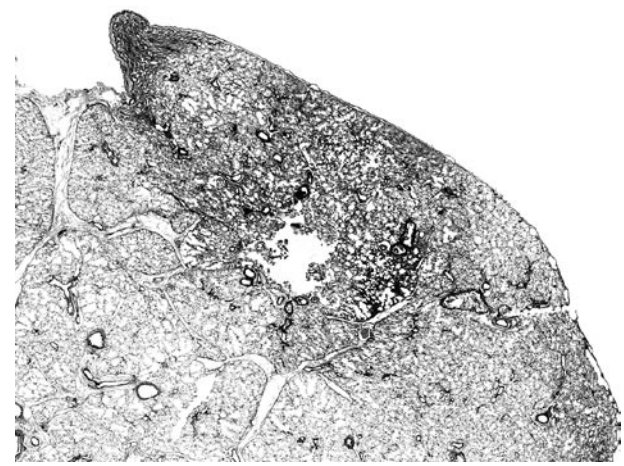


FIGURE 3-1 *Fractures of bones of the thoracic cage may lead to missile-like injuries of the lungs.* ***(A)*** *Interspersed bone fragment within the pulmonary tissue in an explosion-related fatality.* ***(B)*** *Higher magnification of the same bone fragment. Note the lamellar structures and Haversian canals on the surface clearly identifying this foreign body as a bone fragment. Hematoxylin & Eosin.*

FIGURE 3-2
Missile track in a case of penetrating lung injury. Note the extension of the hemorrhagic destruction zone towards the subpleural lung segments. (Scanning of a large-section histological preparation of lung parenchyma.) Periodic acid-Schiff.

After opening of the chest cavity at autopsy in cases of penetrating lung injury following explosions, one can see round to oval, reddish-bluish bruising zones shining through the surface of the pleura visceralis around both entry and exit wounds of the lungs. On cut sections through the lungs as well on the large-section histological preparations, mantle-like bleeding zones radially surrounding the missile track can be seen in cases of penetrating lung injury (see Figure 3-2). Alveolar tears showing club-shaped distensions of ruptured alveolar septa with consecutive enlargement of alveolar spaces (see Figure 3-3) and intraalveolar hemorrhages are the main light microscopical findings in these mantle-like bleeding zones surrounding the missile track radially (Tsokos, Sperhake & Paulsen 2005). These club-shaped distensions of ruptured alveolar septa represent a special feature of alveolar architectural damage that can be explained by the dynamics of temporary cavitation: radial acceleration and overdistension of tissue during temporary cavity formation initiates stretch mechanisms of the displaced tissue, causing the alveolar



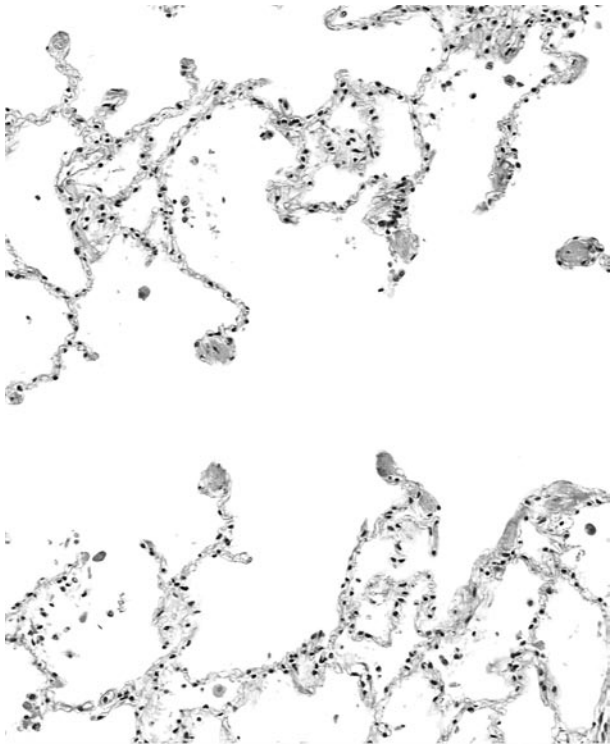


FIGURE 3-3
Pulmonary tissue destruction following penetrating lung injury: club-shaped distensions of ruptured alveolar septa with consecutive enlargement of alveolar spaces. Hematoxylin & Eosin.

septa to rupture with subsequent foreshortening and pursing of elastic alveolar fibers. When the temporary cavity subsides, leaving the permanent cavity, club-shaped distensions of the ruptured alveolar septa remain as a result of this structural alveolar damage (Tsokos et al. 2005).

Following an explosion, inhalation of hot noxious gaseous products of detonation and/or combustion leads to edema, mucosal bleeding, and patchy or vesicular detachment of the mucosa of the trachea and bronchi.

Aspiration of soot or blood in the airways (see Figures 3-4 to 3-6) is another frequent finding in both survivors and deceased. As an marker of inhalation before death, the presence of soot and/or blood in the airways proves that the victim was alive at the time of the explosion. It has to be emphasized that no significant amount of soot can pass the vocal cords and enter the trachea after death. In contrast, blood may run down the trachea postmortem. However, the finding of aspirated blood within the alveoli, appearing as a circumscribed reddish-violet mosaic of blood deposits on cut sections throughout the lung parenchyma at autopsy, proves that the deceased was at least breathing (either being conscious or unconscious) at the time of the explosion. Most often the finding of aspiration of a large quantity of blood is associated with fractures of the base of the skull with opening into the naso- and oropharynx following blunt force trauma to the head caused by the explosion (from e.g., tertiary or quarternary blast injury). On the other hand mild to moderate hemorrhage into the bronchi and circumscribed (focal) blood deposits in alveolar spaces do not necessarily have to originate from aspiration of blood from a bleeding source situated above the trachea or main bronchi, but may also derive from damaged capillaries located in the interalveolar septae or larger interstitial vessels.

Following penetrating or blunt trauma to the lungs, an increased pulmonary leukocyte sequestration, margination, and emigration can be observed

as early as 20 to 30 min after the trauma (Obertacke et al. 1998; Rainer et al. 2000). After isolated unilateral lung contusion, an increase in leukocyte sequestration in the contralateral (unaffected) lung does not occur until 8 hr after the initial traumatic lung injury (Obertacke et al. 1998). In missile injuries of the lungs, involvement of the contralateral (unaffected) lung has to be considered a secondary event caused by a systemic inflammatory reaction, potentially leading to rapid respiratory deterioration with progressive acute respiratory distress syndrome (ARDS) (Tsokos et al. 2005).

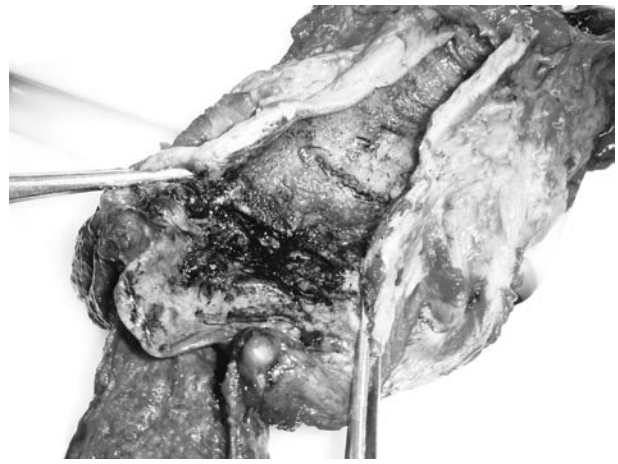
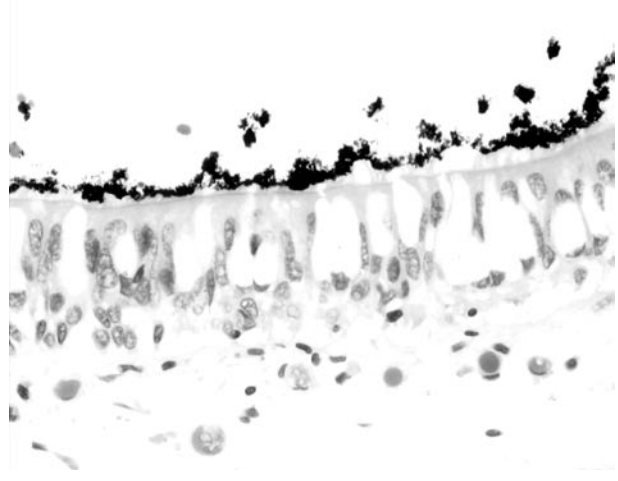


FIGURE 3-4
Aspiration of soot in the larynx. A thick layer of soot is covering the laryngeal mucosa.

Those who survive blast exposure are likely to develop ARDS and sepsis. Of course, causes of ARDS other than blast lung injury or other traumatic lung injuries such as hypovolemic shock, fluid transfusion, or sepsis may be responsible for development of this lung disorder and the related clinical signs and symptoms, but clinical evidence suggests that the severity of blast lung injury has a dominant effect whether or not ARDS develops in survivors of explosions. However, the postmortem appearance will be much the same, whatever the cause of ARDS. The autopsy features of the lungs in ARDS are as follows: At gross inspection, the lungs appear in a gloomy bluish-reddish color. The weight of the lungs is increased due to pulmonary edema, congestion, and pulmonary trapping of inflammatory cells. The lung parenchyma appears usually wet with muddy-grayish fluid draining from the cut sections of the lungs due to accumulation of protein-rich edema fluid in the alveolar spaces and interstitium. At microscopic examination, interstitial (perivascular and peribronchial) edema and intraalveolar fibrin deposits are found in earlier stages of ARDS, followed by a protein-rich intraalveolar edema. Plasma proteins, cellular debris and fibrin deposits

FIGURE 3-5
Histological appearance of soot aspiration in the trachea in an explosion-related fatality. Hematoxylin & Eosin.



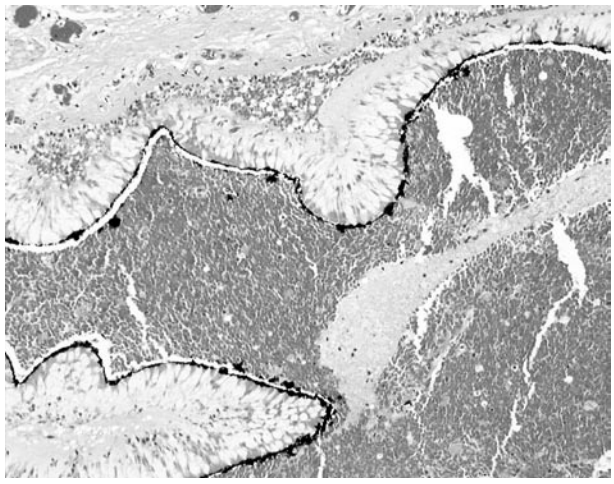


FIGURE 3-6
Aspiration of blood and soot in a smaller bronchi. Blood cells as a result of blood aspiration are present within the lumen and black, amorphous material (soot) is covering the epithelial layer of the bronchus. Hematoxylin & Eosin.

covering the alveolar epithelium as hyaline membranes (see Figure 3-7) and interstitial deposition of inflammatory cells as well as interstitial fibrosis are findings indicative of ARDS in advanced stages (Martin, Soloway & Simmons 1968; Schlag et al. 1993; Tsokos 2005).

BLAST LUNG INJURY

The pathophysiology of blast lung injury differs significantly from all other forms of lung trauma. Human blast lung injury represents a pattern of lung pathology *sui generis*. Due to multiple reflections of the blast wave off walls and obstacles, thus creating a complex and longer lasting blast wave pattern, victims of explosions in confined spaces have a higher incidence of blast lung injury and a higher mortality rate in comparison with victims of explosions who were injured in the open air. The exact mechanisms involved in lung injury from blast wave exposure are not yet completely understood. As a result of blast wave exposure, high velocity longitudinal pressure waves propagate through the body, thus leading to pressure differentials at the interface between tissues with different densities (Phillips 1986; Mellor 1988; Cooper & Taylor 1989; Stuhmiller et al. 1996). Reflection of stress waves off the mediastinum and the thoracic cavity is considered to cause complex pressure conditions within the lung parenchyma, which reinforce pressure differentials at barriers of different densities, thus causing the alveolar septae and walls of capillaries to rupture (Cooper et al. 1983; Mellor 1992).

In the clinical setting, in victims of explosions, the diagnosis of "blast lung" is usually made by the presence of dyspnea and cough that develop to a rapid respiratory deterioration with progressive hypoxia and subsequent ARDS. The diagnosis is confirmed by chest radiographs showing the characteristic butterfly appearance of the lungs. Blast lung patients may present with or without pneumothorax, and smoke inhalation of the upper airways is a frequent finding at bronchoscopy (Caseby & Porter 1976; Phillips 1986; Katz et al. 1989; Leibovici et al. 1996). Pizov and coworkers (1999) studied blast lung injury deriving from explosions in confined spaces in a clinical series of 15 patients. Out of the 15 patients,

seven had bilateral pneumothoraces and five developed ARDS during their clinical course. In eight patients, radiographic findings were characterized by diffuse bilateral opacity, strongly suggesting intrapulmonary hemorrhage.

Blast lung injury is the major cause of death in patients who survive initial resuscitation (Mellor 1988, 1992; Mellor & Cooper 1989). Early mortality is associated with air emboli and massive pneumothorax and hematothorax (Pode et al. 1989).

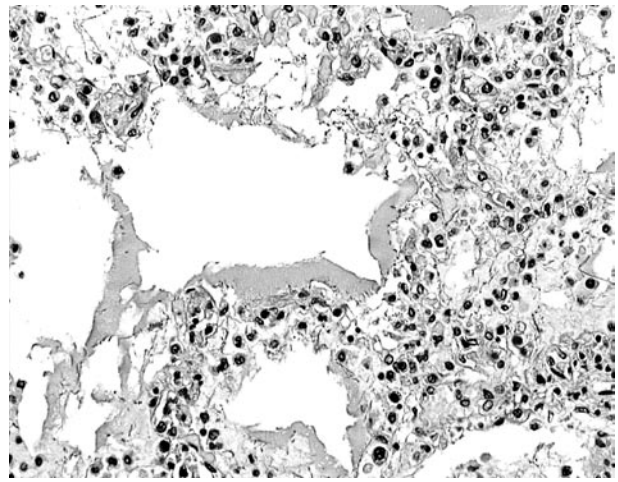


FIGURE 3-7
Hyaline membranes covering the alveolar epithelium in acute respiratory distress syndrome. Hematoxylin & Eosin.

Pathological Features

Although bombing incidents are prone to be highly variable concerning scene settings, number of victims, and explosive chart properties, the pathological features of human blast lung injury are always much the same on both the macroscopical and microscopical level.

Gross Pathology

Blast lung injury is usually accompanied by other lung injuries not due to primary blast effects (see earlier). If pneumothorax (unilateral or bilateral) is not present, after opening of the thoracic cavity at autopsy, the lungs usually show severe overdistenstion at gross inspection. Grossly visible lesions of the lungs are circumscribed or more confluent petechiae as well as pulmonary hemorrhages seen under the pleural surfaces or within the parenchyma on cut sections through the lungs. These pulmonary hemorrhages may be arranged in a focal, multifocal, or diffuse pattern (Elsayed 1997; Mayorga 1997). Subpleural pulmonary hemorrhages are occasionally accompagnied by tense hemorrhagic bullae.

Although some authors have described blast lung injury as always associated with edema of the lungs, it has to be emphasized strongly that a pulmonary edema can only be observed in blast lung specimens if the affected individual survived blast wave exposure for quite a while. If present, the intensity of lung edema is positively correlated with the length of the survival time of the patient. At gross inspection, lung edema manifests as frothy grayish-reddish fluid draining from the cut sections of the lungs at autopsy.

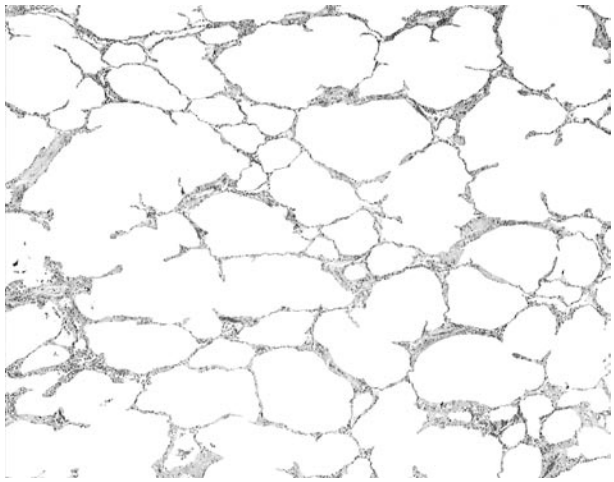


FIGURE 3-8
Histopathology of human blast lung injury. Panoramic view of severe alveolar overdistension: enlargement of alveolar spaces, ruptures, and thinning of alveolar septae. Hematoxylin & Eosin.

Histopathology

Human blast lung injury displays a relatively uniform picture in the early stages of the disease.

When the blast wave reaches an interface between areas of differing acoustic impedance, part is reflected and part continues. Pressure differentials (stresses) occur at the interface between media with different densities. These stresses are most marked at air/fluid interfaces. In the lung, the pressure differentials across alveolar/capillary interfaces lead to rupture of the alveolo-capillary barrier, thus resulting in the typical appearance of blast lung injury under the microscope (see Figure 3-8). Alveolar ruptures, thinning of alveolar septae and enlargement of alveolar spaces are the distinctive histopathological findings of blast lung injury. Marked congestion of pulmonary arteries, arterioles, veins, venules, and alveolar capillaries accompanied by vascular engorgement is another frequent, although not obligatory, finding (see Figure 3-9).

As mentioned earlier, pulmonary edema is not a typical pathological feature of blast lung injury. A mild to moderate amount of eosinophilic deposit filling the alveolar spaces and interalveolar septae corresponding to edema fluid is seen in those cases with survival times of up to a few hours. A more intense alveolar and interstitial edema as well as additional leukostasis within the pulmonary microvasculature accompanied by a sparse interstitial inflammatory infiltrate can be observed in blast lung victims with longer survival times.

Circumscribed subpleural, intraalveolar and perivascular hemorrhages, the latter usually showing a cuff-like pattern in the interstitial spaces around larger and smaller pulmonary vessels (see Figure 3-10) are further histopathological findings frequently seen in blast lungs. The microscopical detection of circumscribed interstitial hemorrhages within the lung parenchyma from blast victims without coexisting blunt or penetrating chest trauma provides evidence that pulmonary vessels have to be regarded as potentially life-threatening intrapulmonary bleeding

sources that might require thoracotomy immediately after admission (Inoue et al. 1993, Matsumoto et al. 1998). Whether these perivascular hemorrhages are a result of pressure differentials and therefore a direct primary blast effect or if these lesions derive from shearing forces affecting the lung parenchyma when the lung is abruptly decelerated on the interior chest wall after acceleration due to the indirect blast wave effect remains unclear at present (Tsokos et al. 2003a).

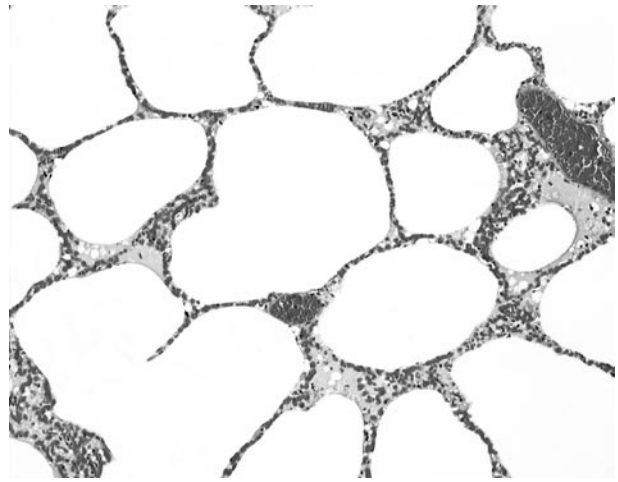
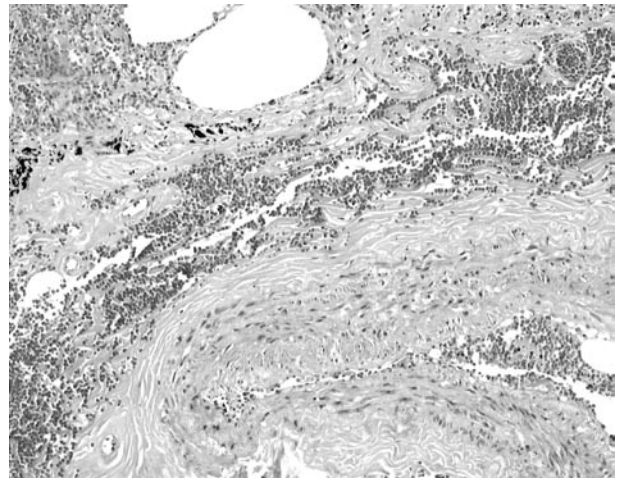


FIGURE 3-9
Congestion and vascular engorgement of alveolar capillaries and smaller interstitial vessels in a human blast lung. Hematoxylin & Eosin.

Venous air embolism is another well-recognized histopathological feature of blast lungs (Tsokos et al. 2003a). Venous air embolism is considered the major factor leading to cardiac dysfunction and immediate death after blast wave exposure (Phillips 1986; Mayorga 1997; Argyros 1997). It has been a matter of debate over the last decades whether air embolism in blast victims represents only an artifact caused iatrogenically by mechanical ventilation. However, a recent autopsy-based study provided evidence that blast-related air embolism is most probably originating, at least to a certain degree, from entry of air either from blast-induced enlargement of airspace with consecutive rupture of alveolar walls and absorption of air into the adjacent pulmonary veins, or from tears of the pulmonary parenchyma as a result of tertiary blast effects causing blunt thoracic trauma (Tsokos et al. 2003a).

FIGURE 3-10
Interstitial perivascular hemorrhage showing a cuff-like pattern around a larger pulmonary artery. Hematoxylin & Eosin.

Pulmonary bone marrow embolism (see Figure 3-11) and fat embolism (see Figure 3-12) are additional histopathological findings occasionally seen in those who died from blast lung injury (Tsokos et al. 2003a).



Immunohistochemistry

Recent evidence suggests that, as alveolar septae and alvolar capillary walls rupture as a result of blast wave exposure and intraalveolar hemorrhage occurs, red blood cells also rupture and release hemoglobin (Hb),

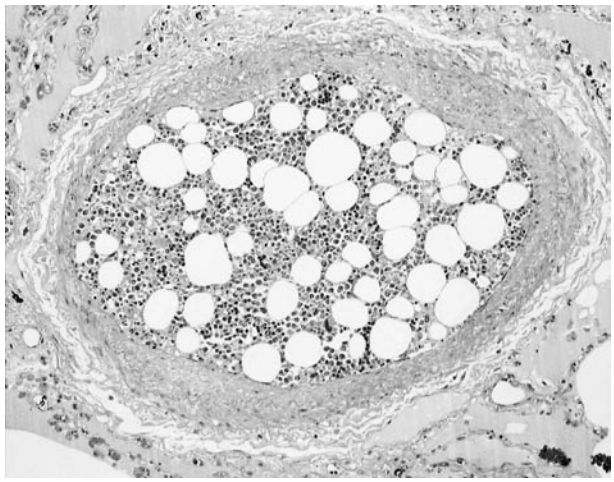


FIGURE 3-11
Microscopical appearance of bone marrow embolism: hemopoietic cells and fat droplets occluding a pulmonary artery. Hematoxylin & Eosin.

which in turn amplifies the cascade of events leading to oxidative stress (Elsayed, Gorbunov & Kagan 1997). This assumption has been confirmed recently on the micromorphological level: a homogenous Hb immunoreactivity has been found within the intraalveolar edema fluid in blast lung fatalities without evidence of any Hb immunopositive erythrocytic cell structures in marked contrast to a strong Hb immunopositivity restricted to erythrocytes within the alveolar edema fluid in hemorrhagic (toxic) lung edema from controls (see Figure 3-13) (Tsokos et al. 2003a).

Ultrastructural Appearance of Human Blast Lung Injury

Scanning electron microscopical studies have confirmed the observations made on the light microscopical level, namely that alveolar ruptures with enlargement of alveolar spaces and thinning of alveolar septae constitute the main morphological feature of blast lungs (see Figure 3-14). In addition, small perforations of the alveolar wall measuring between 0.5–9 μm in diameter can be detected at higher magnification.

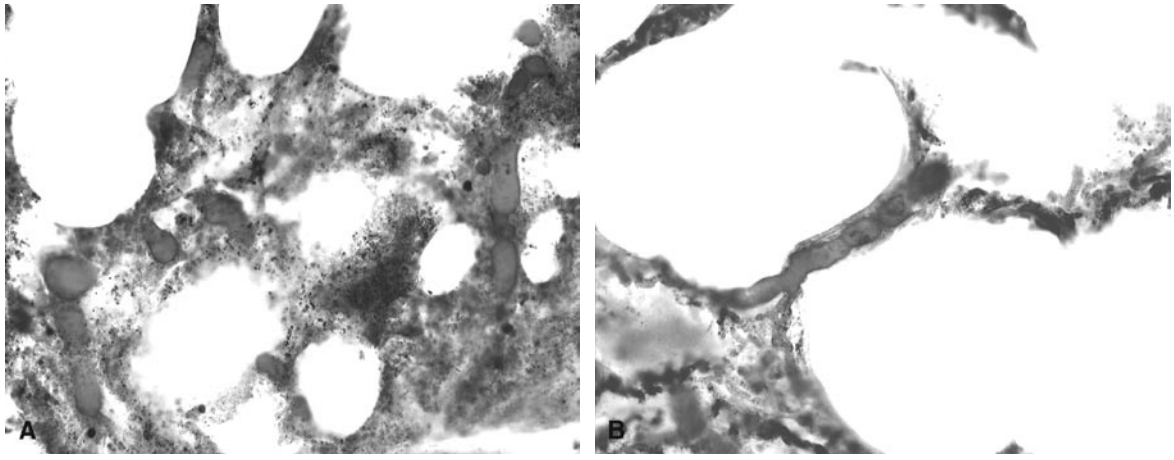


FIGURE 3-12 *Pulmonary fat embolism in human blast lung injury **(A)** Droplets of fat deposits (pulmonary fat embolism grade I) and sausage-shaped fat deposits (grade II) within smaller pulmonary vessels and alveolar capillaries **(B)** Grade III pulmonary fat embolism: Antler-shaped fat deposit occluding an alveolar capillary. Fat Red 7B.*

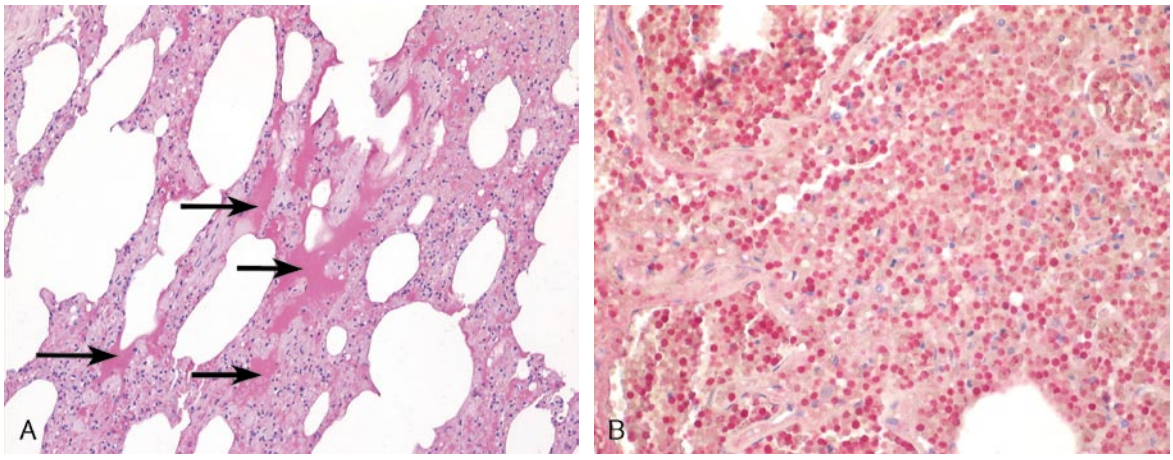


FIGURE 3-13 *Immunohistochemical staining for hemoglobin (Hb)* ***(A)*** *Human blast lung injury: strong Hb immunoreactivity of edema fluid (arrows) within alveolar spaces* ***(B)*** *Control subject: Strong Hb immunopositivity restricted to intact erythrocytes within the alveolar edema fluid in a nonblast case; this subject died from hemorrhagic (toxic) lung edema.*

CONCLUDING REMARKS

Victims of explosions usually suffer from a combination of blast lung injury, blunt force trauma, penetrating injuries, and burns. The type, distribution, and severity of injuries of bombing victims most often indicate their location in relation to the epicenter of explosion. Although the particular environment within which an explosive device detonates significantly influences the pathology of injuries caused by explosives, the pathological features of human blast lung injury following explosions are always much the same.

Human blast lung injury represents an exceptional and unique pattern of lung pathology not comparable to any other spectrum of natural or nonnatural lung disease encountered by both clinicians and pathologists. The main micromorphological features of human blast lung injury can be summarized as follows: homogenously distributed severe alveolar overdistension with alveolar ruptures, thinning of alveolar septae and enlargement of alveolar spaces

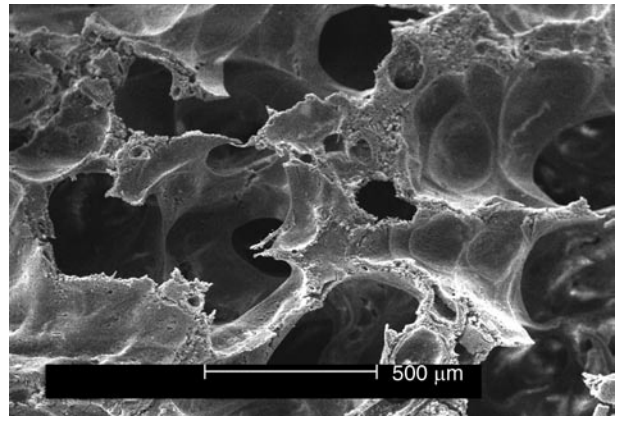


FIGURE 3-14 *Scanning electron microscopical image of human blast lung injury: Alveolar ruptures and enlargement of alveolar spaces.*

as well as subpleural, intraalveolar, and more circumscribed perivascular, cuff-like hemorrhages. The intensity of pulmonary edema in blast lung injury is positively correlated with the length of the survival time of victims of blast wave exposure. Those who survive blast exposure are likely to develop ARDS and sepsis. Clinical evidence suggests that the severity of blast lung injury has a dominant effect whether or not ARDS develops in survivors of blast wave exposure.

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CHAPTER 4

Neurotrauma from Explosive Blast

Geoffrey Ling, Faris Bandak, Gerald Grant, Rocco Armonda, and James Ecklund

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Types of Traumatic Brain Injury
Severity of Traumatic Brain Injury
Prevalence
Mechanisms of Injury
Blast Mechanics
Blast Injury
Clinical Management
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Conclusion
Disclaimer

INTRODUCTION

Explosive devices have been used as weapons since the invention of gunpowder. The current conflicts in Iraq and Afghanistan are no different, except they have highlighted the use of devices referred to as IEDs (improvised explosive devices) where it has been reported they cause over 60% of combat casualties (Shanker 2007).

U.S. and European military experience traditionally has indicated that head trauma is common among injuries incurred in combat. During the Vietnam War, approximately 15 to 20% of wounds sustained by U.S. servicemen in

combat involved the head. Of all casualties who died after reaching medical care, almost half were due to traumatic brain injuries (TBI). In more recent conflicts like the first Gulf War, there were far fewer U.S. casualties than in wars past. However, even then, head trauma still accounted for about 15% of all combat-related injuries. The epidemiologic data is still evolving for Operation Iraqi Freedom (OIF) and Operation Enduring Freedom in Afghanistan (OEF). However, early evidence suggests that injury patterns of these modern wars are similar to those noted for previous conflicts (Bellamy, Maningas & Vayer 1986; Carey 1996; Bellamy 1992).

Throughout modern history, the source of war-related TBI remains largely explosive ordinance. Overwhelmingly, penetrating head injury is a result of shrapnel projectiles penetrating the skull with bullet penetration wounds being significantly less frequent (Carey 1996; Bellamy 1995). However, in war as in the civilian experience, TBI can also occur without a penetrating head wound and at all severity levels. This also includes being exposed just to the explosive blast (Warden 2006).

The advances in protective body armor have contributed greatly to the reduced mortality among current U.S. warfighters. Unfortunately, even this effective equipment cannot fully prevent TBI. The modern protective vest or individual body armor (IBA) is successful in protecting the torso. Penetrating injuries to the chest and abdomen have been dramatically reduced from past conflicts. Coupled with improved medical care, the modern U.S. military now experiences one of the lowest killed-to-wounded ratios (less than 1 in 10 patients die) in its history. A consequence of this is that more warfighters are surviving what previously would have been fatal injuries. Thus, other injury conditions like TBI from explosive blast (bTBI) are now becoming relatively more prominent than they had been before (Zoroya 2005).

The modern combat helmet is an excellent protective device. It can mitigate injury from most forms of low velocity projectiles such as shrapnel, and under certain circumstances, high velocity projectiles such as bullets. However, it does not cover the face, lower back of the neck, or lower side of the head. In these unprotected areas, injury occurs (Jaffe 2004).

TYPES OF TRAUMATIC BRAIN INJURY

Traumatic brain injury is traditionally classified as resulting from penetrating or closed head injury. Closed head injury (CHI) refers to injury where

the cranium remains intact and where the dura has not been breached. This is also referred to as blunt head injury. Concussion is the classic example of CHI. Typically, CHI is caused by head impact from falls, violence, sports, and more commonly from motor vehicle crashes. In CHI, the disruption in brain function is due to the brain motion and deformation within the cranium, resulting in the classically observed injuries to the brain parenchyma, blood vessels, and fiber tracts.

Penetrating head injury (PHI) involves disruption of the cranium with concomitant dural breach. Typically, this injury results from a projectile that violates the bony skull and then passes through the brain parenchyma. Pathology is a result of physical disruption of neuronal cells and fiber tracts exacerbated by ischemia and hemorrhage. The events most commonly associated with PHI involve bullet, knife, shrapnel, and the like.

Emerging evidence suggests that there may be another class of head injury, bTBI. Blast TBI involves disruption of brain function following exposure to an explosion. Patients who suffer bTBI may have an intact calvarium, but not always. Typically, their injuries result from explosive forces transmitted transcalvarially into brain parenchyma. The forces responsible for bTBI are generally not well understood but overpressure, electromagnetic energy, acoustics, and others all have been implicated as potential etiologies. The agent most commonly associated with bTBI is high explosive ordnance.

SEVERITY OF TRAUMATIC BRAIN INJURY

TBI is defined as traumatically induced physiological disruption in brain function such that there is loss of consciousness (LOC), loss of memory preceding or following injury (amnesia), alteration in mental status at time of injury, and/or focal neurological deficit (Mild Traumatic Brain Injury Committee 1993). TBI severity can be classified as mild, moderate, or severe. Mild TBI is a brief (<5 min) loss of consciousness or awareness. Typically, patients also complain of headache, confusion, and amnesia. Other symptoms that may occur include difficulty concentrating, mood alteration, sleep disturbance, and anxiety (Report of the Quality Standards Subcommittee 1997). These often resolve within a few hours or days. A postconcussive syndrome of delayed symptoms may develop. This delayed syndrome can be treated with nonnarcotic analgesics, antidepressants,

and conservative therapy. Typically, it will last a few weeks but, in some cases, can persist up to a year or more (Alexander 1995).

Moderate TBI is associated with a presenting Glasgow Coma Score (GCS) of 9 to 13, often with prolonged loss of consciousness and/or neurological deficit (Geocadin 2004). Patients suffering from moderate TBI will require hospitalization and may need neurosurgical care. They too may develop postconcussive syndrome.

Severe TBI occurs when a patient is obtunded or comatose. They suffer from significant neurological injury to the extent that their presenting GCS is 8 or less, often with abnormal neuroimaging, like a CT scan revealing fracture or hemorrhage (Geocadin 2004). These patients require advanced medical care, which commonly includes airway protection, mechanical ventilation, neurosurgical intervention, intracranial pressure monitoring, and treatment in an intensive care unit setting. Recovery is prolonged and usually incomplete if at all. A significant percentage of severe TBI patients will not survive to 1 year (The Multi-Society Task Force on PVS 1994).

Concussion, a subtype of CHI, can also be classified as mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild concussion is defined as a brief confusion lasting less than 15 minutes but no loss of consciousness. Moderate is when a patient has a period of confusion that lasts longer than 15 minutes but still does not experience loss of consciousness. Severe concussion is whenever there is any loss of consciousness (Report of the Quality Standards Subcommittee 1997).

A new taxonomy for bTBI is being proposed. Mild bTBI is defined as loss of consciousness less than one hour and posttraumatic amnesia less than 24 hours. Moderate bTBI is loss of consciousness for more than one but less than 24 hours and amnesia lasting more than one but less than seven days. Severe bTBI is loss of consciousness over 24 hours and amnesia over seven days. It should be understood that this classification has not yet gained wide acceptance in the medical community (Okie 2005; Warden & French 2005).

PREVALENCE

Numerous articles in the popular lay media have reported prevalence of bTBI approaching 40 to 60% of deployed U.S. warfighters (Shanker 2007;

Zoroya 2005, 2007). The evidence supporting these claims is limited. To date, there has not been a comprehensive scientifically rigorous epidemiological study conducted on this condition. Instead, the data used to generate these conclusions are from single center studies. Some of these studies rely on self-reported data and others, on narrow inclusion criteria (Okie 2005; Zoroya 2006). Care must be taken when trying to generalize such data. It is unclear how many of these patients suffered bTBI versus other injury, such as falling or other accidental injury. Without necessarily suffering overt physical injury, others may have suffered psychological injury due to the personal experience or from witnessing severe injury inflicted on fellow soldiers. Identifying primary blast injury in isolation without other causal factors present is difficult. Often, patients with definite bTBI suffer from other injuries, mostly to the extremities, that are so severe that these patients require evacuation from theater. As such, it is highly probable that many may have been physically thrown or exposed to explosive ejecta (e.g., shrapnel). Thus, trying to quantify the contribution of blast alone to this complicated clinical picture is difficult (Warden 2006; Zoroya 2005, 2007).

MECHANISMS OF INJURY

There has been much reported on the causes and mechanisms of bTBI. Specifically, cause is the action generated by the blast and mechanism is the interaction of the blast with the human body resulting in injury (i.e., how the body is injured). Typically, in trauma, there are primary and secondary injury mechanisms. Primary injury mechanism is the basis of the primary injury and is that attributed directly to the action of the cause. For example, the physical energy (cause) generated by a swinging fist (mechanism) strikes the eye leading to a bruise around the eye (primary injury). Secondary injury can also result, which is from the consequent pathophysiological changes following the primary injury (the swelling that develops overnight around the "black eye"). Of course, it is probable that bTBI is not restricted to a single injury mechanism. In blast, there are likely several potentially coupled mechanisms. For example one mechanism can be interpreted from the direct blast shock wave impinging directly on the head and another could be from the same shock wave impinging on the whole body. Together, they contribute to the bTBI syndrome.

BLAST MECHANICS

A blast is a pressure phenomenon referring to the propagation of a disturbance in a medium such as air or water. One process by which a blast is generated involves the explosion or detonation of an energetic material referred to as a conventional (versus nuclear) explosive. This material essentially provides highly efficient storage of molecular binding energy in a relatively small volume but has the important characteristic of relative instability. This large quiescent stored chemical energy, which is confined in a relatively small volume, can be released very rapidly when a chemical reaction is induced. This energy release is associated with a phase change generating rapidly expanding gas that transfers mechanical energy into the surrounding volume as well as into objects or people within it. The extent and intensity of this process for each explosive is dependent on several factors such as size, chemical content, confinement, and so on. This rapid, chemically-driven expansion is a "detonation."

An important feature of an explosion is that the expansion involves the rapid displacement of air resulting in pressure waves that can travel faster than the sound speed and therefore become shock waves. The free-field shock wave leads the decaying pressure disturbance consisting of different wave speeds and different peak pressures as described by Friedlander, who also showed that the rapid pressure rise is followed by slow decay in pressure that may rebound to below the previously undisturbed ambient levels. This is more complicated in the nonfree field (enclosed) conditions where the pressure waves can reflect off of walls, structures, barriers, and other objects. These reflections give rise to a "complex wave field." Such circumstances usually are analyzed on an individual basis without the generalization of a single relation such as Friedlander's. Here the contributions from the shape and the peak of each of the components of the complex wave has a part to play and should be accounted for in the assessment of injury.

BLAST INJURY

There are four categories of blast injury. The first or primary are injuries that are due only to exposure to the explosive detonation. Secondary injuries are caused by propelled objects like shrapnel. Tertiary are those injuries resulting from the patient being physically thrown (e.g., head striking

a wall). The fourth and last category includes all the injuries resulting from other remaining explosive related factors, such as burns, inhalation of toxic fumes, and such. This discussion focuses mainly on primary blast (2006).

Various injury mechanisms have been postulated for blast and include those related to different tissue densities, air-filled organs, shear, and tensile stresses. Such mechanisms are thought to be activated as a result of the blast shock and/or overpressure (Bowen et al. 1968; Richmond et al. 1968). Clear description of the activation and operation of these mechanisms has not yet been reported. The resulting injuries however, have been reported across body region affecting the thoracic, abdominal, head, ears, and central nervous system.

Blast overpressure is hypothesized by many investigators as the leading cause of blast-related injury. Early animal studies report that increasing peak pressure is associated with increased mortality (Bowen et al. 1968; Richmond et al. 1968). As lungs are air-filled organs, they are considered the most susceptible tissue to overpressure effects. From the preclinical experiments, it is widely held that pulmonary failure is what leads to blast-related death (Philips & Richmond 1991). In trauma, severe pulmonary injury manifests as Acute Respiratory Distress Syndrome (ARDS). From the OIF and OEF experiences, isolated ARDS following explosive blast injury is rare even though neurological effects are not. These clinical findings raise the possibility that overpressure alone is not the only mechanism by which blast leads to injury (Okie 2005; Ling & Maher 2006).

CLINICAL MANAGEMENT

The essentials of bTBI management are the same as other types of TBI. Proper clinical care begins in the field and starts with the "ABCs" of airway, breathing, and circulation (Knuth et al. 2005), after which, the patient's GCS should be determined. In isolated head injury, the GCS can be helpful in making triage decisions. If GCS is impaired, patients should be taken to higher levels of care. Certainly if GCS is 13 or less, this should be expeditious; for example, by helicopter air evacuation (Knuth et al. 2005). However, IED blast injuries are complex and often result in multiple injuries requiring simultaneous management (Knuth et al. 2005).

After arriving at a higher echelon of care, more detailed clinical assessment should be made. Neuroimaging should be done early to identify lesions such as intracranial hemorrhage, skull fracture, cerebral edema, and others. Such conditions may require early neurosurgical intervention. Additionally, all TBI patients should be managed according to the established standard of care guidelines for clinical management of this condition. The critical issues are maintaining adequate oxygenation, controlling intracranial pressure (ICP), ensuring proper cerebral perfusion pressure, and so on. Delayed intracranial hypertension is common in severe bTBI. Patients have been noted to develop increased ICP 14 to 21 days after severe bTBI. One medical therapy that has been used with great success in these types of injuries is hypertonic saline. Intravenous boluses of 23% NaCl can be used for acute elevations of ICP with continuous intravenous infusions of 2% and 3% NaCl solutions to maintain ICP control. Other therapies that have been promising in mitigating delayed intracranial hypertension are hypothermia (34°–36°C) and early decompressive craniectomy (Geocadin 2004; Ling & Maher 2006; Knuth et al. 2005; Brain Trauma Foundation 2000; Ling & Ecklund 2007; Ling 2007; Battlefield Advanced Trauma Life Support 2001).

Following a penetrating blast injury to the brain, the majority of military patients undergo a decompressive craniectomy. Experience has shown that early hyperemia and severe cerebral edema frequently occur in the setting of a significant blast injury. Thus, a decompressive craniectomy permits the swelling brain to avoid compression by the bony skull. From a practical military standpoint, craniectomy provides an additional measure of safety for intracranial pressure (ICP) control through the evacuation process where, at times, ICP management can be challenging. The other benefit of early decompressive craniectomy is that it may obviate the need to use more conventional methods of ICP control such as pharmacological coma. Barbiturate coma is difficult to execute in the deployed setting due to the limited number of neuro-critical-care specialists and lack of EEG support. Thus, for many reasons, decompressive craniectomy is the most practical, if seemingly aggressive, approach (Okie 2005; Schlifka 2007; Grant 2007).

IED blast injuries are multifactorial. There is soft issue trauma from the blast with possible severe facial and scalp burns. There is primary blast injury due to the severe concussive blast wave for which the underlying

mechanism is poorly understood. Clinically, it may range from mild to severe with diffuse axonal injury. Secondary blast injuries are common and include open depressed skull fractures from penetrating fragments. Tertiary blast injury can also occur from the head striking a solid object leading to a CHI. Also there can be skull base injuries to the middle fossa, temporal bone, or frontal sinus that should be suspected if patients have otorrhea or rhinorrhea. Finally, there can be critical vascular effects of both arterial and venous origin, such as sagittal sinus injury and lacerated cortical arteries. These latter injuries have a high risk for traumatic pseudoaneurysm formation. Blast related pseudoaneurysms have been observed to expand in spite of endovascular ablation attempts. Thus, patients with such lesions often require craniotomy and aneurysm clipping (Armonda et al. 2006).

Vasospasm is a particularly common finding after bTBI. Recent work by Armonda et al. (2006) reveal that up to 50% of patients suffering moderate to severe bTBI developed cerebral vasospasm. Early transcranial Doppler studies in theater reveal that this vasospasm can develop early, often within 48 hours of injury (Ling & Ecklund 2007). Vasospasm can also present later in the course of this disease, typically 10 or more days after initial injury. Patients who are considered higher risk based on the trajectory of the penetrating fragments or blast injury also get imaging studies to follow their propensity for pseudoaneurysm formation. However, the efficacy of CT-angiogram may be limited as some pseudoaneurysms evade diagnosis when using this modality. At the National Naval Medical Center and Walter Reed Army Medical Center, traditional four-vessel cerebral angiography is the more favored diagnostic approach.

The decision to aggressively remove shrapnel debris or bone fragments lodged in the brain has evolved since the Vietnam and Korea Wars. Previously, surgeons aggressively sought to remove all foreign bodies including the bone fragments in an effort to reduce the infection risk and the risk for development of posttraumatic epilepsy. Follow-up on treated Vietnam War patients and other more recent studies from other conflicts have shown that aggressive removal of all fragments is unnecessary, but removal of gross contamination with debridement of large injury tracts is beneficial. Currently, any accessible fragments are removed that can be safely debrided along the tract, but fragments that may be deep or subcortical, contralateral, or otherwise inaccessible, are left in place. The reconstruction

of the dura and scalp closure is important to reduce the incidence of cerebrospinal fluid (CSF) leak and meningitis. A soldier who presents with a GCS 15 and has small penetrating fragments in the brain will likely get a local debridement of the scalp so long as there is no CSF leak. On the contrary a soldier who presents with a GCS 3 with a large penetrating fragment will likely undergo a large decompressive craniectomy with removal of the fragment despite the poor prognosis for neurological recovery (Schlifka 2007; Grant 2007; Carey et al. 1972, 1998).

There is a heightened concern for Acinetobacter and other infections, many of which are prevalent in Iraq and are often drug resistant. Due to the high incidence of concomitant skull base trauma and CSF leak following the blast injuries, patients may have complex Leforte fractures as well as a ventriculostomy, lumbar drain, or both in place. Early maxillofacial fixation is performed, even in the setting of a head injury. The compounded morbidity of drug-resistant Acinetobacter baumannii meningitis with external drains in place is much greater than early surgical intervention. Anecdotal reports suggest that early reduction of the facial fractures has been effective in minimizing CSF leaks.

BLAST CONCUSSIVE INJURY

A difficult aspect of bTBI that results in mild TBI or concussion is diagnosis. Early recognition of concussion is critical to ensure that the warfighter gets timely medical care and is not returning to duty with compromised mental status, which is often subtle. In a deployed environment, first providers are medics who may not have sufficient training in recognizing the subtleties of mild TBI. Warfighters suffering mild TBI typically do not have overt evidence of trauma (e.g., lacerations, hematomas, etc.). The patient him- or herself may not recognize that he or she has suffered an injury. Thus, there needs to be a heightened awareness that this condition might exist in a soldier who has been exposed to an explosive blast such that the medic will undertake appropriate clinical investigation. If warranted, the warfighter should be referred to higher echelons of care, ideally to a neurologist, neurosurgeon, or emergency medicine physician (Warden 2006; Ling & Maher 2006).

Many soldiers may not seek medical care after their first blast exposure as they do not recognize that they may have been injured. It may not be until

after the second or third blast exposure that they will realize that they may have been injured. Also, medical providers may not recognize their symptoms as resulting from explosive blast. Patients can complain of persistent postconcussive symptoms, such as headaches, vertigo, short-term memory loss, or difficulty concentrating or multitasking (Okie 2005; Ryan & Warden 2003; Ropper & Gorson 2007). Since many of these symptoms can be fairly subtle, these soldiers should undergo a comprehensive extensive evaluation by a physician or psychologist. Objective neuropsychological testing is needed and, even though it may consist only of limited bedside testing, that may be sufficient. Efforts are underway to develop neuropsychological test batteries that can be automated on a laptop computer or are easy enough to be applied by less trained providers. Balance plate testing also is being studied as a surrogate marker of mild TBI. The benefit of balance plate testing is that it is noninvasive, reproducible, objective, and easy to administer (Zoroya 2000).

A particularly vexing issue is the potential overlap of mild TBI with posttraumatic stress disorder (PTSD). PTSD signs and symptoms share many clinical features as mild TBI. Some symptoms common to both are difficulty concentrating, mood lability, sleep disruption, and increased anxiety (Association 2000). Furthermore, some injured warfighters may suffer simultaneously from both PTSD and TBI (Ropper & Gorson 2007; Warden et al. 1997). Therefore, soldiers with these signs also should be evaluated by a combat stress team provider or psychiatrist.

If TBI is suspected, the patient should be removed from combat-related duties. This may mean light duty for a period of time until symptoms fully resolve or evacuation out of theater to a higher echelon of care where advanced neuroimaging and more detailed evaluation may be instituted.

Second Impact Syndrome (SIS) needs to be avoided. SIS is a condition that can develop if a subsequent head injury occurs before full recovery (Ling 2007). This can lead to worse clinical outcome. In the very young, SIS is associated with a high mortality rate. The American Academy of Neurology has published guidelines for concussion management that includes recommended periods of recovery. Other guidelines can also be used, such as the Cantu Grading system and the Colorado Medical Society Guidelines. Although developed for sports-related TBI, these provide some meaningful reference for military health care providers (Ling 2007;

Ropper & Gorson 2007; Bailes & Cantu 2001; Bleiberg et al. 2004). There is presently a Triservice effort in the United States to improve the education of providers and medics prior to deployment. This effort has heightened the awareness for detecting these injuries despite the subtle signs and symptoms in a deployed setting. A large prospective observational clinical study under the auspices of the Defense and Veterans Head Injury Center is underway to follow these soldiers closely and validate the objective neuropsychological testing to help formulate triage decisions.

CONCLUSION

Blast TBI is another element in the overall disease of TBI. It shares many features of traditional TBI but does have unique aspects. It also shares many features of PTSD but hereto has unique aspects. Rigorous scientific study at both the basic science and clinical levels are needed. It must include improved understanding of the cause and mechanisms by which explosive blast leads to TBI. A comprehensive epidemiological study is desperately needed so as to determine the prevalence of this disease and the factors that contribute most to the risk of developing the disease. A clear clinical description of bTBI with diagnostic criteria would greatly improve diagnosis. It is only through disciplined and focused research that meaningful prevention, mitigation, and treatment strategies for bTBI can be realized.

DISCLAIMER

The views and opinions expressed herein are those of the authors and do not reflect those of the Department of the Army or the Department of Defense.

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CHAPTER 5

Effects of Blast Injury on the Autonomic Nervous System and the Response to Resuscitation

Emrys Kirkman, Sarah Watts, Wayne Sapsford, and Marina Sawdon

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Summary

Disclaimer

INTRODUCTION

Blast injury refers to the biomechanical and pathophysiological changes and the clinical syndrome resulting from exposure of the living body to detonation of high explosive. Although some aspects of blast injury have been well known for centuries, others were not well recognized or scientifically

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investigated until World War I (Hooker 1924; Mott 1916; Rusca 1915). Since then groups in the United Kingdom, Germany, and the United States studied the effects of free-air and underwater blasts on animals (Barrow & Rhodes 1944; Benzinger 1950; Cameron, Short & Wakely 1942; Desaga 1950; Greaves et al. 1943; Rossle 1950; Zuckerman 1940). The advent of nuclear weapons, with blast waves of very long duration, and the secondary effects of the explosions (collapse of buildings, the generation of missiles and burns, the translational effects, and radiation effects) further stimulated work, especially at the Lovelace Foundation in the United States (Bowen, Fletcher & Richmond 1968; Fletcher & Bowen 1968; Richmond et al. 1968; White et al. 1971). In the United Kingdom and other countries, research was directed toward combating the threat from terrorist atrocities involving explosive devices (Cooper et al. 1983; Hadden, Rutherford & Merrett 1978). More recently, the development of fuel-air and thermobaric explosive devices (Dearden 2001; Galbraith 2001; Savic, Ignjatovic & Mrdja 1990) and their currently limited use in modern theaters of war has led to a renewed interest in the effects of blast injury on the human body. Blast injuries continue to be an important cause of both military (Montgomery, Swiecki & Shriver 2005; Nelson et al. 2006) and civilian trauma (Almogy et al. 2005; de Ceballos et al. 2005; Marti et al. 2006; Ryan & Montgomery 2005).

Classification of Blast Injuries

Blast injuries fall into three main categories (Maynard, Cooper & Scott 1989; Zuckerman 1941): primary, secondary, and tertiary with miscellaneous additional injuries forming a further group (see Table 5-1).

Table 5-1 Classification of Blast Injuries

Type of Blast Injury	Cause of Injury	Main Organs Affected
Primary	Direct impact on tissues of shock waves emanating from an explosion	Lung Gastrointestinal tract Ears Paranasal sinuses
Secondary	Fragments, missiles, flying objects, and other energized debris	Solid organs Central nervous system
Tertiary	Physical displacement of the whole or part of the body	Central nervous system Skeletal system Solid organs
Miscellaneous	Flash burns, fire, noxious hot gases, dust, crush injury, drowning, and psychological problems	

Primary blast injuries result from the interaction of a shock wave with the body. Injury is largely confined to the air-containing organs, such as the lungs, bowel, and ears, often without external signs of injury (Clemedson 1956), although recently there is heightened suspicion that primary blast may also cause brain injury (Belanger et al. 2005; Lew et al. 2006; Okie 2005).

Secondary blast injury results from the impact of fragments and larger missiles accelerated by the blast. The source of these missiles may be the device itself—its casing or contents such as ball bearings or nails—or from the environment within which the device detonates and may include stones, glass, brick, metal, and wood. Injuries caused by these fragments can be further categorized as penetrating or nonpenetrating. This group accounts for the majority of blast injuries, particularly in open spaces.

Tertiary blast injury results from the acceleration of the whole body or parts of the body by the blast wave causing translational impacts of the body with the ground or other fixed objects, and/or traumatic amputation of body parts and stripping of tissue. A further group of miscellaneous injuries includes flash burns, caused by the radiant and convective heat of the explosion; burns caused by the combustion of the environment; crush syndrome; and the effects of noxious gaseous products liberated in enclosed spaces, especially carbon monoxide and psychological effects.

The relative frequency of each type of injury is difficult to predict and depends on the quantity and type of explosive, the construction of the explosive device, the proximity of the casualty to the source of the explosion, and the environment within which the charge detonates. Very close to the detonation of a condensed explosive, a victim is likely to die from bodily disruption. Further away, there will be a fatal combination of primary blast injury, secondary fragment injury, and tertiary injuries. As the distance increases the effects of fragment injury in personnel predominate and, in general, this form of injury is the most common in military and civilian bombings. At long distances from the source, the effects of primary injury (this time exclusively auditory) become preeminent because the hazard from fragments reduces as they are widely dispersed and travel at low velocities at long ranges. However, novel munitions such as fuel-air and thermobaric explosives are designed to maximize primary and tertiary injury over wide areas due to their prolonged shock wave overpressures

dispersed over large areas (Dearden 2001), and primary blast injuries are more common in confined spaces due to reflection and amplification of the shock wave.

PRIMARY BLAST INJURIES

Blast lung is the most notable primary blast injury (see Figure 5-1). Blast lung is characterized by contusions of the lungs in which blood contaminates the alveoli (usually without parenchymal laceration). The contusion may range from scattered petechiae to confluent hemorrhages involving the whole lung. The contusions may be bilateral, but frequently they are confined to the lung facing the blast (see Figure 5-1A) and they may continue to spread over the ensuing hours and days (Cooper 1996). A physiological shunt may be established and the lung compliance will decrease, resulting

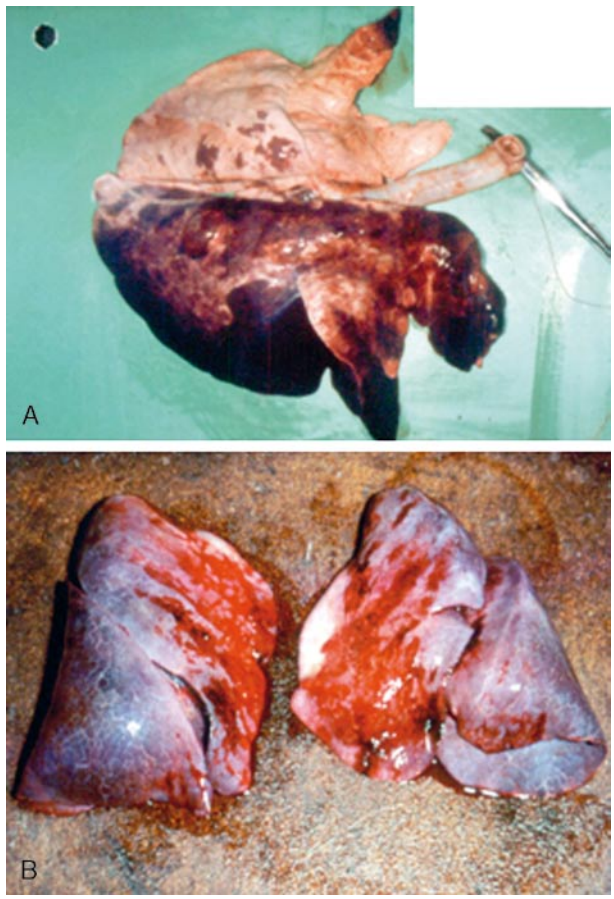


FIGURE 5-1
*Photographs showing characteristic blast lungs **(A)** from a terminally anaesthetized pig exposed to detonation of a single charge (2.2 kg of EDC1) at a range of 1.5 m from the center of the charge to the outside of the chest wall. The animal was lying supine and exposed to blast from the right side. Note the pulmonary contusions especially on the right side. **(B)** Postmortem lungs from a human blast victim. Note the extensive pulmonary contusions and the characteristic rib markings that are now believed to be intercostal space markings.*

in stiffer lungs and hypoxia (Cohn 1997). The injury may progress to acute respiratory distress syndrome (ARDS) (Cooper et al. 1991), often within 24 to 48 hours (Gans & Kennedy 1996; Mellor 1988) with the worst of the respiratory distress and hypoxemia being seen within the first 72 hours (Cohn 1997; Gans & Kennedy 1996; Mellor 1988; Argyros 1997; Frykberg, Tepas & Alexander 1989; Katz et al. 1989; Leibovici et al. 1996).

Physiological Response to Primary Blast Injury

Primary blast injury results in a characteristic cardiorespiratory response that is mediated in large part by the autonomic nervous system. However, it must also be recognized that other mechanisms such as the release of mediators (e.g., nitric oxide) into the circulation may also play a significant role in the acute response to blast injury.

The inherent problems of clinical observations following blast in humans have resulted in the most reliable physiological data being derived from animal studies. Most of the early animal work involved exposing animals to the effects of the detonation of high explosives, either in the open or in shock tubes to create blast waves of varying amplitude and duration. These experiments were necessarily carried out in an environment that limited the application of precise technology in the study of the pathophysiological effects of primary blast injury. Later developments involved the use of a bench-top shock wave generator such as that developed at DSTL Porton Down (see Figure 5-2) (Jaffin et al. 1987). Both models have utility depending on the nature of the question being addressed. However, important differences need to be noted with respect to interpreting data using these different models. The bench-top apparatus is capable of producing blast waves focused on well-defined aspects of the body and allows detailed continuous physiological monitoring while blast is being applied. This model, therefore, is particularly suited to the study of the regional effects of blast and the body's response to these insults. It is a necessary starting point for complex mechanistic studies of the response to blast that represents an interaction of responses initiated when a range of body areas are exposed to blast. In addition it allows investigation of which component(s) of the response to blast interact with responses to other clinically relevant insults (e.g., hemorrhage or musculoskeletal injury). By contrast, experiments using high explosives generally involve the exposure of the entire body to blast and, hence, include inherent interactions between the responses generated by regional blast exposure. Although this

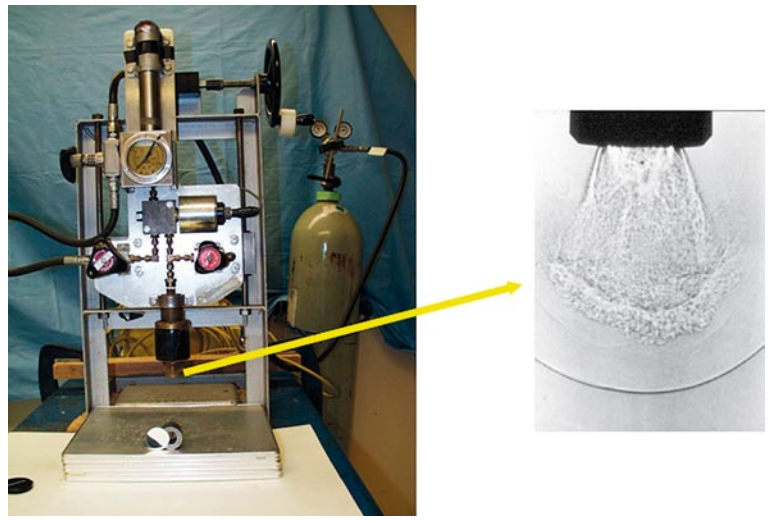


FIGURE 5-2 *Photograph of bench-top blast generator developed at Porton Down. A compressed air cylinder containing air is connected to the apparatus. When a solenoid is opened the air is admitted to a chamber resulting in the rupture of an aluminum bursting disk, directing a shock wave (insert) to an anesthetized animal beneath. The resulting shock wave can be directed toward specific anatomical regions (e.g., thorax, abdomen, or head). Note the shock wave followed by the turbulent movement of gas emanating from the blast nozzle in the panel on the right.*

does not allow the dissection of the mechanistic interactions between the responses to various blast injuries it does allow an examination of the interaction between a general blast response and other insults such as blood loss. These factors, together with the usual physiological considerations of species and effects of anesthesia must all be considered when evaluating data where animals are used to model the human condition.

Cardiorespiratory Response to Primary Blast Injury to the Thorax

A number of experimental studies and clinical reports indicated that primary blast injury to the thorax produces bradycardia (Barrow & Rhodes 1944; Cernak et al. 1996; Clark & Ward 1943; Clemedson 1949; Irwin et al. 1997; Guy et al. 1998), prolonged hypotension (Barrow & Rhodes 1944; Cernak et al. 1996; Clemedson 1949; Irwin et al. 1997; Guy et al. 1998), and apnea followed by rapid shallow breathing (Jaffin et al. 1987; Clark & Ward 1943; Clemedson 1949; Guy et al. 1998) (see Figure 5-3). Initially, it was thought that the bradycardia was a preterminal event, possibly associated with cessation of coronary blood flow (Krohn, Whitteridge

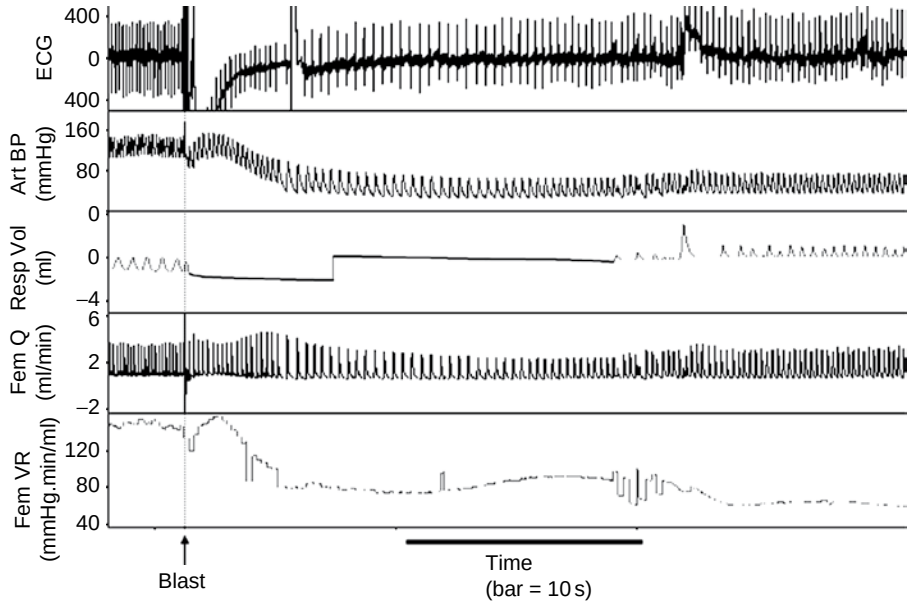


FIGURE 5-3 *Typical effects of a single blast exposure to the thorax of an anaesthetized male Wistar rat on the electrocardiogram (ECG), systemic arterial blood pressure (Art BP), respiratory tidal volume (Resp Vol, inspiration upward), femoral arterial blood flow (Fem Q), and femoral vascular resistance (Fem VR). The animal was terminally anesthetized with alphadolone/alphaxolone (21 mg.kg^{-1}.h^{-1}) and a single blast wave from a bench-top apparatus (Figure 5-2) was applied to the ventral thorax at the point indicated (Blast).*

& Zuckerman 1942). However, more recent studies have demonstrated that the bradycardia is a consistent finding following thoracic blast, even in animals that survive (Guy et al. 1998), and that it is an autonomic reflex.

Time Course and Reflex Nature of the Acute Cardiorespiratory Response to Thoracic Blast Injury

A detailed study of the immediate response to primary blast injury to the thorax has shown that the cardiovascular and respiratory responses are not instantaneous; the bradycardia had a latency of onset of approximately 4 sec, and blood pressure began to fall approximately 2 sec after blast (Ohnishi et al. 2001). This latency is consistent with the response being reflex in nature rather than being the consequence of direct effects (e.g., on the heart or CNS). The initial bradycardia was seen to resolve quickly after blast although some degree of bradycardia persisted for up to 1 hr after thoracic blast, and hypotension persisted for at least 2 hr (see Figure 5-4).

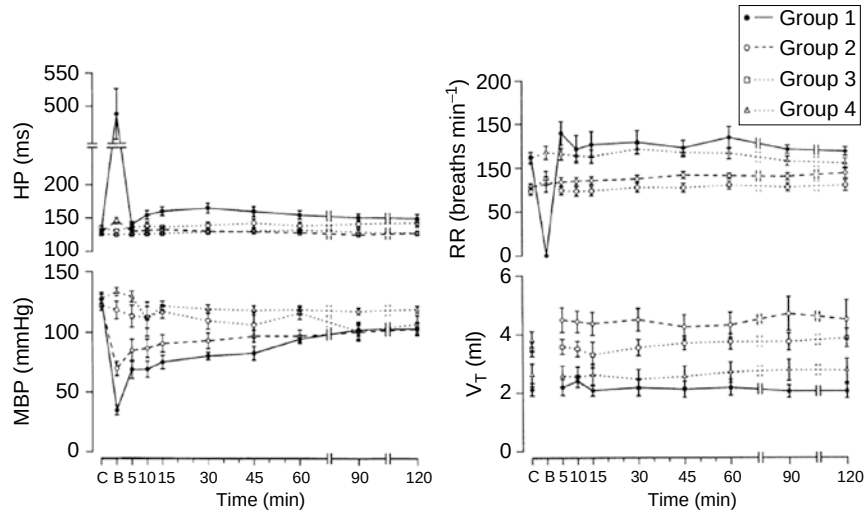


FIGURE 5-4 *Cardiovascular and respiratory effects of exposure to a single blast directed toward the ventral thorax in terminally anaesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg.kg^{-1}.h^{-1}). HP, heart period (time interval between heart beats); MBP, mean arterial blood pressure; RR, respiratory rate; VT, respiratory tidal volume recorded before blast (C), the peak effect of blast (B), and thereafter at the times indicated after blast. The groups were treated as follows: Group 1, sham vagotomy then thoracic blast, n = 8; Group 2, cervical vagotomy then thoracic blast, n = 8; Group 3, vagotomy then sham thoracic blast, n = 8; Group 4, sham vagotomy then sham thoracic blast, n = 8. Data are mean ± s.e.mean. From Ohnishi et al. (2001).*

More recent studies have shown that the response also includes a reduction in vascular resistance, at least in skeletal muscle (see Figure 5-3). Coincident with the cardiopulmonary changes there are early and prolonged falls in arterial oxygen tension following thoracic blast (see Figure 5-5) consistent with the development of pulmonary edema (Damon et al. 1971). $PaCO_2$ may fall if pulmonary edema is mild or may rise with more severe pulmonary edema after severe blast injury since pulmonary transfer of carbon dioxide is affected less by edema than the transfer of oxygen. These changes are associated with increases in lung weight indices and lung dry/wet weight ratios, both of which are consistent with the development of pulmonary edema.

Contribution of the Autonomic Nervous System to the Cardiorespiratory Response to Primary Blast Injury

The cardiorespiratory response to blast injury is a reflex involving the vagus nerve (e.g., see Krohn et al. 1942; Ohnishi et al. 1998, 2001; Irwin

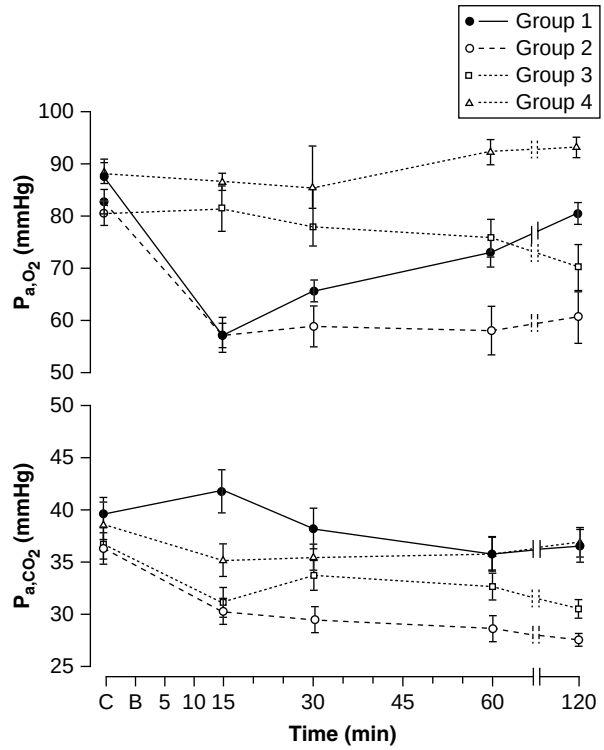


FIGURE 5-5

Blood gas changes after exposure to a single blast directed toward the ventral thorax in terminally anaesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg. $kg^{-1}.h^{-1}$). PaO_2 and $PaCO_2$, arterial oxygen and carbon dioxide tensions, respectively, recorded before blast (C), the peak effect of blast (B), and thereafter at the times indicated after blast. Details of group treatments are as given in Figure 5-4. Data are mean ± s.e. mean. From Ohnishi et al. (2001).

et al. 1999). The efferent and possibly the afferent pathways mediating the bradycardia is vagal since the fall in heart rate can be abolished by atropine or vagotomy (see Figures 5-4, 5-6) (Ohnishi et al. 2001). The apnea is also entirely a vagal reflex as it can be abolished by vagotomy (see Figure 5-4) (Ohnishi et al. 2001).

The etiology of the hypotension seen after primary blast injury is complex. The fall in blood pressure appears to be due to a fall in peripheral resistance and cardiac output, the latter because of a myocardial impairment (see Figure 5-7). Although the autonomic nervous system plays some part in the hypotension it is clearly not solely responsible. Evidence that there is a reflex element to the hypotension is provided by the finding that vagotomy attenuates the fall in blood pressure seen after blast (Ohnishi et al. 2001) (see Figure 5-4). The contribution of the vagus to the hypotension is not via the bradycardia since atropine, which blocks the bradycardia, does not attenuate the hypotension (Ohnishi et al. 2001). Consequently it is likely that the afferent fibers in the vagus may initiate a reflex that results in hypotension. One potential mechanism is a reflex

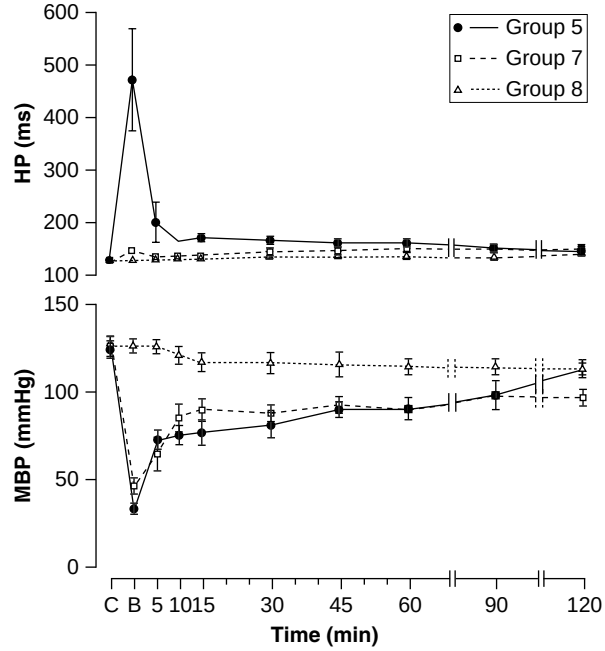


FIGURE 5-6 *Effects of atropine on the cardiovascular effects of exposure to a single blast directed toward the ventral thorax in terminally anaesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg.kg^{-1}.h^{-1}). HP, heart period (time interval between heart beats); MBP, mean arterial blood pressure recorded before blast (C), the peak effect of blast (B), and thereafter at the times indicated after blast. The groups were treated as follows: Group 5, 0.9% saline (1 ml.kg^{-1} i.v.) then thoracic blast, n = 9; Group 7, atropine (0.3 mg.kg^{-1} i.v.) then thoracic blast, n = 8; Group 8, atropine (0.3 mg.kg^{-1} i.v.) then sham thoracic blast, n = 8. Data are mean ± s.e.mean. From Ohnishi et al. (2001).*

inhibition of sympathetic vasoconstrictor tone, such as occurs when the pulmonary afferent C-fibers are activated (Daly & Kirkman 1987, 1988). However, removal of sympathetic control of vascular resistance with guanethidine (in a preparation with sufficient vascular tone to demonstrate the response to blast) did not attenuate the fall in vascular resistance seen after blast, suggesting that a reflex withdrawal of sympathetic vasoconstrictor tone does not play an important part in blast-induced hypotension (Ohnishi & Kirkman, unpublished observations). More recent findings have suggested an alternative mechanism to account for the vasodilator response. It has now been shown that primary blast injury causes a rapid release of the potent vasodilator nitric oxide (NO) from the pulmonary circulation (Gorbunov et al. 2006; Zunic et al. 2000, 2005). It is

thought that such a brisk overproduction of NO could lead to a systemic response that includes vasodilatation (J.L. Atkins, personal communication).

Finally, in addition to the reduced vascular resistance, myocardial impairment (resulting in reduced cardiac output) may also contribute to the hypotension. Cardiac index and left ventricular stroke work index have been shown to be depressed for at least 6.5 hours after blast injury (see Figure 5-7) (Harban et al. 2001). It is currently unclear whether the release of NO and the myocardial depression are related or the extent to which the autonomic nervous system contributes to these changes.

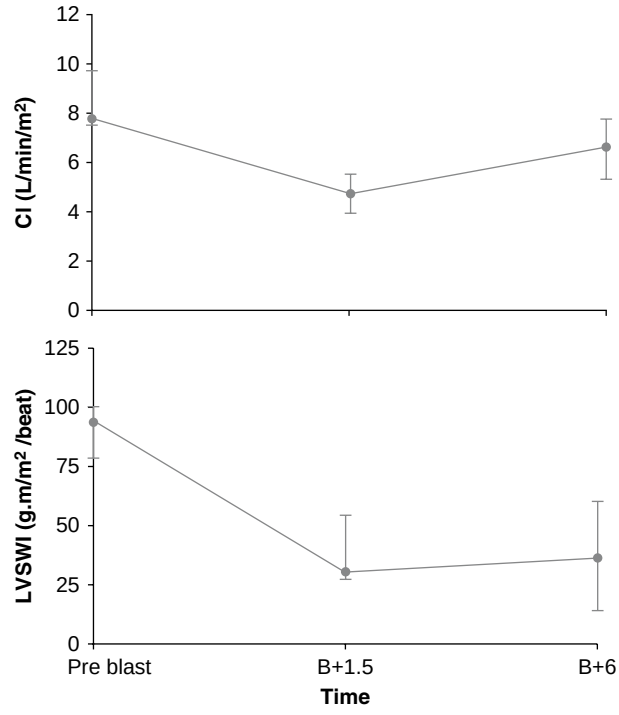


FIGURE 5-7

Effects of primary blast injury due to single blast exposure on myocardial performance in vivo in a group of terminally anesthetized large white pigs. CI, cardiac output indexed to body weight; LVSWI, left ventricular stroke work index. Data were recorded before blast and thereafter at 1.5 and 6 hours postblast (B+1.5 and B+6 respectively). Data are median (interquartile range). Data taken from Harban et al. 2001.

Although the reflex mediating the response to thoracic blast has not been fully characterized, the response has many similarities to that induced by activation of the pulmonary afferent C-fibers (Daly & Kirkman 1987, 1988). The pulmonary afferent C-fibers can be activated mechanically (e.g., by an increase in pulmonary interstitial pressure or volume) or chemically by $5HT_3$ agonists acting in the pulmonary circulation (Daly & Kirkman 1988). The rapid onset of the reflex response suggests that it is not due to pulmonary edema, which would be expected to have a more gradual onset. One possibility was that the blast injury caused the release of serotonin from platelets in the pulmonary circulation that in turn initiated the reflex response. This hypothesis was tested by investigating the effects of blocking pulmonary $5HT_3$ receptors with ondansetron prior to blast exposure. However, ondansetron ($100\ \mu g.kg^{-1}$), a dose that blocked the effects of the $5HT_3$ agonist phenylbiguanide on the pulmonary C-fiber reflex, did not block the cardiorespiratory response to thoracic blast (Ohnishi et al. 1998). Hence it was concluded that the cardiorespiratory response to thoracic blast injury is not mediated by local release of serotonin in the lungs (Ohnishi et al. 1998). The mechanism of activation and precise nature of the afferent pathway mediating the reflex response to primary blast injury

therefore are currently unknown. A possibility that remains to be tested is whether the rapid (transient) change in pressure caused as a shock wave traverses the lung is capable of producing the brief, intense, stimulation of the pulmonary afferent C-fibers that would initiate the reflex response to primary blast injury.

In summary, thoracic, but not abdominal (Guy et al. 1998), blast produces a triad of bradycardia, hypotension, and apnea. The bradycardia and apnea are mediated entirely by a vagal reflex, the most likely candidate being the pulmonary afferent C-fiber reflex. The hypotension appears to be mediated by a reduction in vascular resistance as well as a fall in cardiac output. By 30 minutes after blast the reduction in vascular resistance is reversed but the myocardial depression seems to persist, contributing to long-term hypotension.

Pharmacological Modulation of the Response to Primary Blast Injury

Drugs may be given to a blast casualty, or given to an individual who later becomes a blast casualty, for reasons that are not directly connected with blast injury. Other drugs could be given in an attempt to treat some aspects of the response to blast.

Interaction with Drugs Given for Purposes Unrelated to Blast

Pyridostigmine

Pyridostigmine is a prophylactic agent given to those at risk of exposure to chemical agents with anticholinesterase activity (i.e., the so-called nerve agents) (Dawson 1994; Gunderson et al. 1992). Since pyridostigmine itself affects reversible blockade of acetylcholinesterase (hence, protecting it from irreversible blockade by nerve agents), it was not surprising to discover that pyridostigmine pretreatment markedly increased the vagally mediated bradycardia induced by thoracic blast (see Figure 5-8). Pyridostigmine, however, did not increase the hypotension or apnea, which are not mediated by cholinergic mechanisms. Thus, individuals pretreated with anticholinesterase agents are likely to display exaggerated bradycardic responses to blast.

Morphine

Activation of central μ opioid receptors is known to attenuate some vagally-mediated reflexes such as the baroreflex (Eltrafi, Kirkman & Little 1988)

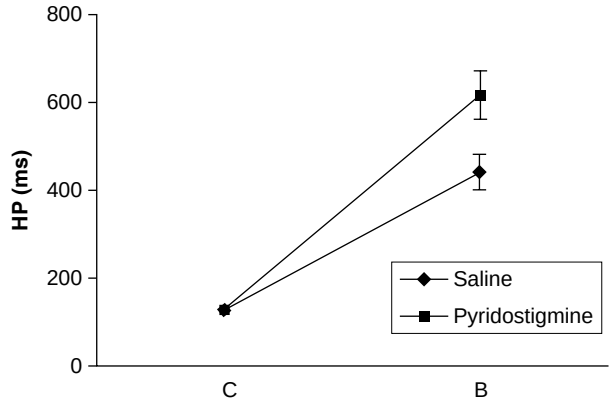


FIGURE 5-8 *Effects of pyridostigmine on the bradycardia resulting from exposure to a single blast directed toward the ventral thorax in terminally anesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg.kg^{-1}.h^{-1}). The animals were treated with either pyridostigmine bromide (18.6 μg.h^{-1}) or 0.9% saline (1 μl.h^{-1}) continuously for 7 days before being exposed to a single blast to the ventral thorax. HP, heart period (time interval between heart beats) recorded before blast (C), the peak effect of blast (B). The groups were treated as follows: 0.9% saline and thoracic blast, n = 9; Pyridostigmine and thoracic blast, n = 9. Data are mean ± s.e.mean.*

and the bradycardic response associated with severe hemorrhage (Ohnishi et al. 1997, 1998). In addition, activation of μ receptors can also lead to respiratory depression (Hruby & Agnes 1999; White & Irvine 1999). Since the response to thoracic blast injury includes a reflex vagally-mediated bradycardia and apnea (Ohnishi et al. 2001), it may be modified by μ receptor activation with drugs such as morphine or fentanyl. An initial study to test this hypothesis involved pretreatment of animals with morphine before exposure to thoracic blast (Kirkman, Ohniska & Watkins 1999). This study found that although there was some evidence that morphine attenuated the bradycardia immediately after thoracic blast, this was not statistically significant (see Figure 5-9). However, morphine did significantly delay the recovery of blood pressure after thoracic blast in the rat (Kirkman et al. 1999). This latter finding is surprising since morphine is known to attenuate falls in blood pressure after hemorrhage (Ohnishi et al. 1997, 1998). Finally, morphine increased the duration of apnea (68 ± 17 s versus 24 ± 2 s, mean ± s.e.mean, respectively, in morphine and saline treated groups) after blast and prevented the secondary respiratory stimulation, leading to further postblast falls in PaO_2 and increases in $PaCO_2$. These cardiovascular

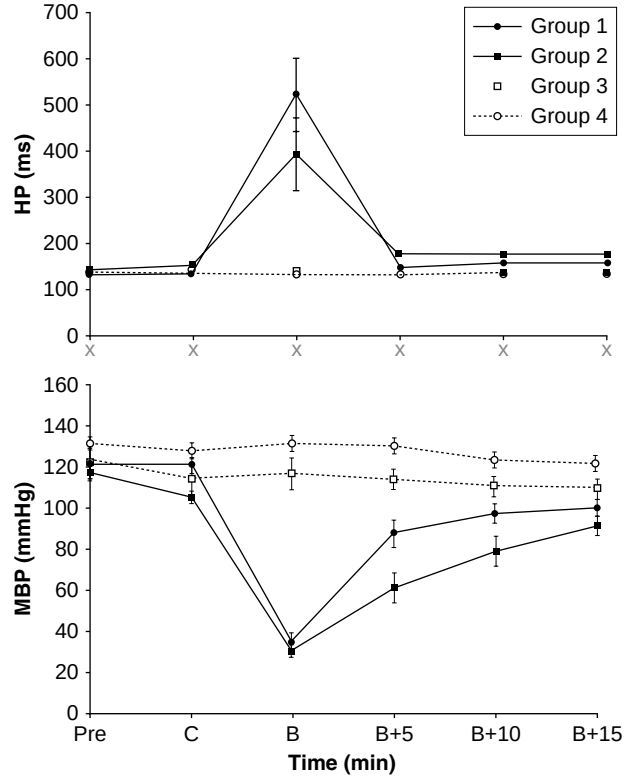


FIGURE 5-9 *Effects of morphine on the cardiovascular effects of exposure to a single blast directed toward the ventral thorax in terminally anaesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg.kg^{-1}.h^{-1}). The animals were treated with either morphine (0.5 mg.kg^{-1} i.v.) or 0.9% saline (1 ml.kg^{-1}) 10–15 min before being exposed to a single blast to the ventral thorax. HP, heart period (time interval between heart beats); MBP, mean arterial blood pressure recorded before blast (C), the peak effect of blast (B), and thereafter at the times indicated after blast. The groups were treated as follows: Group 1, saline then thoracic blast, n = 8; Group 2, morphine then thoracic blast, n = 7; Group 3, morphine then sham thoracic blast, n = 5; Group 4, saline then sham thoracic blast, n = 8. Data are mean ± s.e.mean.*

and respiratory effects could be a problem in the hypotensive blast casualty with impaired pulmonary gas transfer.

The timing of morphine administration, however, seems to be important. Later studies investigating the effects of morphine *after* blast exposure found no evidence of enhanced bradycardia or hypotension (Sawdon et al. 2002). The reason for this difference in the effects of morphine remains to be elucidated.

Potential Pharmacological Treatment of Blast Casualties

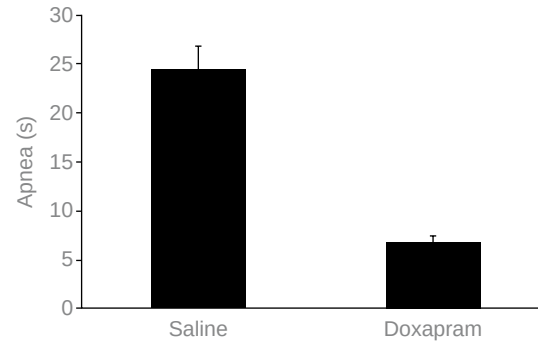
Doxapram

Doxapram is an analeptic (O'Connor, Levy & Peacock et al. 1996) with pressor actions (Bamford et al. 1986). It is used clinically in patients with severe respiratory depression (Angus et al. 1996; Greenstone & Lasserson 2003; Kerr 1997; McNamara & Euerle 1994) and in veterinary medicine to stimulate respiration in apneic new-born lambs (NOAH 2003). A recent study has indicated that doxapram, administered as soon as possible after exposure to thoracic blast in anaesthetized rats, significantly reduced the duration of apnea (see Figure 5-10) and thereafter increased respiratory minute volume (Ohnishi et al. 1998). PaO_2, arterial pH, and base excess were well maintained in the doxapram-treated animals compared to those given saline for periods that exceeded its respiratory stimulant effects (see Figure 5-11). In addition, doxapram significantly attenuated the hypotension following blast but did not modify the bradycardic response (see Figure 5-12) (Ohnishi et al. 1998).

These results indicate that doxapram may be exerting beneficial cardiovascular as well as respiratory effects. The potential benefits of early termination of apnea are obvious, but the possible cardiovascular effects warrant further discussion. A number of studies have shown that attenuation of the hypotensive responses *per se* are not always beneficial (e.g., both the responses to musculoskeletal injury and morphine have been shown to attenuate the hypotension associated with blood loss but increase mortality possibly because of an adverse hemodynamic effect) (Marshall et al. 1998; Rady et al. 1991, 1993, 1996; Tibbs 1956; Overman & Wang 1947; Foex, Kirkman & Little 2004). That doxapram, by contrast, may exert a beneficial effect is suggested by a number of findings. First, although the maintenance of PaO_2 after treatment with doxapram possibly could be due to the increase in respiratory minute volume this is unlikely to be the entire explanation since the beneficial effects on blood gases outlast the effects on respiratory minute volume. In addition, earlier studies have shown that even when there is a reflex increase in respiratory minute volume, PaO_2 still falls after blast injury. Thus, doxapram may be exerting an additional effect on pulmonary hemodynamics, although there is currently no evidence that it reduces shunt in other circumstances

FIGURE 5-10

Effects of doxapram on the apnea induced by a single blast directed toward the ventral thorax in terminally anesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg.kg^{-1}.h^{-1}). The animals were treated with either doxapram (10 mg.kg^{-1} i.v.) or 0.9% saline (1 ml.kg^{-1}) 2–5 sec after being exposed to a single blast to the ventral thorax. Data are mean ± s.e.mean.



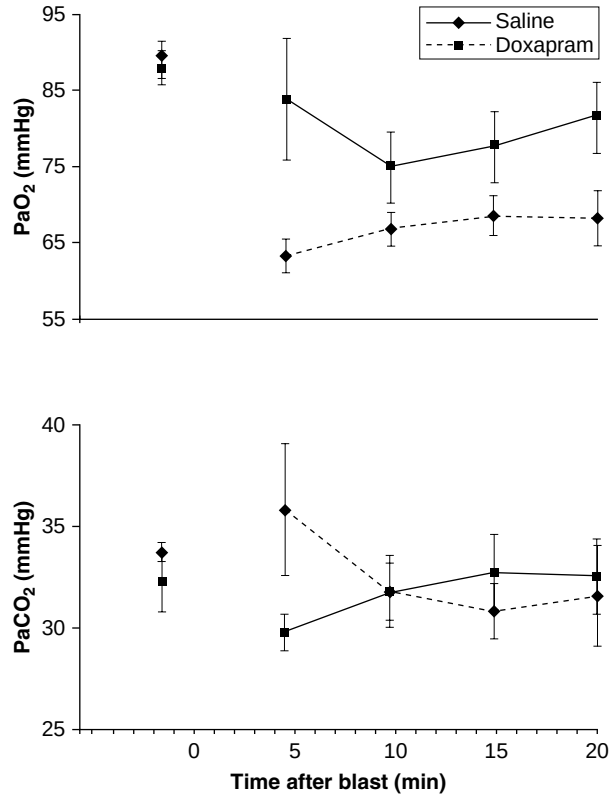


FIGURE 5-11 *Effects of doxapram on blood gas values seen after exposure to a single blast directed toward the ventral thorax in terminally anesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg.kg^{-1}.h^{-1}). The animals were treated as described in Figure 5-10. PaO_2 and $PaCO_2$, arterial oxygen and carbon dioxide tensions, respectively, recorded before blast (C), the peak effect of blast (B), and thereafter at the times indicated after blast. Data are mean ± s.e.mean.*

(Leeman et al. 1992). Furthermore, doxapram may be exerting a beneficial systemic hemodynamic effect, in contrast to other agents that improve blood pressure at the expense of regional blood flow. Thus, the concomitant maintenance of arterial base excess may be due to improved tissue oxygenation not only because of higher PaO_2 levels but also possibly because of improved blood flow to metabolically active regions.

Atropine

Atropine already has been shown to block the bradycardia associated with thoracic blast injury (see Figure 5-6). However, caution should be exercised before employing this treatment as it may cause further problems

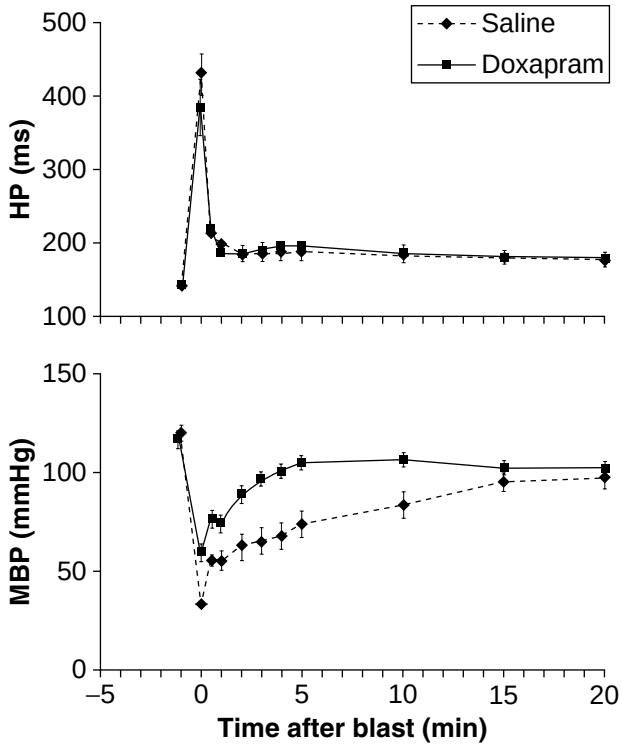


FIGURE 5-12 *Effects of doxapram on the cardiovascular response to a single blast directed toward the ventral thorax in terminally anaesthetized male Wistar rats (alphadolone/alphaxolone 19–12 mg.kg^{-1}.h^{-1}). HP, heart period (time interval between heart beats); MBP, mean arterial blood pressure; RMV, respiratory minute volume recorded before blast (C), the peak effect of blast (B) and thereafter at the times indicated after blast. Data are mean ± s.e.mean.*

for the casualty. Blockade of a vagally mediated bradycardia with atropine under different circumstances, after severe hemorrhage, was found to increase mortality (Barriot & Riou 1987; Barriot, Riou & Buffat 1987).

Death Following Primary Blast Injury

The immediate cause of death following primary blast injury, in the absence of obvious external injuries, has been the subject of much debate in the literature, and a number of theories have been advocated (Benzinger 1950; Clemedson 1949; Krohn et al. 1942; Clemedson & Hultman 1954). Leaving aside deaths due to the total disruption of the body very close to a charge (Krohn et al. 1942) and secondary changes such as the development of ARDS and unrecognized perforation peritonitis, the chief causes

of death will be reviewed. The causes of death can be classified as respiratory and circulatory.

Respiratory Causes

In severe pulmonary blast injury there is massive pulmonary contusion and hemorrhage into the bronchial tree. Bleeding frequently is observed through the mouth and nose (Zuckerman 1940), and the experimental animals are seen to make a few terminal, maximally forced respiratory movements for air as they suffocate in extravasated blood (Zuckerman 1941; Clemedson 1949, 1953, 1956; Krohn et al. 1942). These observations suggest that there is no respiratory center damage (Clemedson 1949) as originally had been suggested by earlier workers (Mott 1916).

In animals that do not obstruct the airways with blood and froth, early pulmonary pathology usually is not sufficient to account for death (Benzinger 1950; Clemedson 1956). The development of pulmonary edema supervening on a physiological shunt through nonaerated contused lung may disturb the pulmonary gas exchange sufficiently to be incompatible with life (Benzinger 1950). Pulmonary edema is, however, a relatively late phenomenon in blast injury (Clemedson 1949). Clemedson supported the view of Benzinger (1950) that respiratory symptoms are not the cause of death but are the consequence of the circulatory failure (Clemedson & Pettersson 1953; Clemedson 1953).

Circulatory Causes

It has been well documented that exposure to blast wave overpressure gives rise to profound changes in the circulatory system. Generally it has been thought that death is secondary to obstruction of the pulmonary capillary bed (Clemedson 1949; Krohn et al. 1942; Clemedson & Hultman 1954; Clemedson & Pettersson 1953) and a greatly dilated right ventricle often is found at postmortem (Clemedson & Hultman 1954). The heart also has been implicated but evidence for *commotio cordis* or sufficient myocardial contusion as the immediate cause of death is scarce (Benzinger 1950; Desaga 1950; Rossle 1950; Clemedson 1949, 1953; Clemedson & Hultman 1954).

Air embolism in blast injury is the result of air entering the circulation through the damaged alveoli (Clemedson & Hultman 1954). In animals dying within some minutes of blast injury, air frequently is found

intravascularly (Benzinger 1950; Rossle 1950; Clemedson & Hultman 1954). The air bubbles are found, often in large quantities, and always in the arterial side of the circulation. Furthermore, air emboli are found only in animals that die rapidly after exposure and never in those animals that survive to be sacrificed (Clemedson & Hultman 1954). Air most commonly is found in the coronary arteries, the left side of the heart, and in brain vessels, especially the basilar vessels and in the choroid plexuses. Therefore, in some cases of immediately fatal primary blast injury, air emboli, especially of the coronary arteries, is likely to be the cause of death. Fat embolism as a cause of death has been suggested (Hooker 1924; Robb-Smith 1941) and refuted (Clemedson 1949; Cohen & Biskind 1946) and the time course of hemorrhagic shock from disrupted solid organs is considered too slow to account for immediate death following blast injury.

The majority of the work on death following primary blast injury was performed in the period after WWII. Modern authors have concentrated on the cardiorespiratory response in sublethal blast exposure and therefore the potential role of the cardiorespiratory response to blast of apnea, bradycardia, and hypotension in immediate death has not received much attention. There is an interesting correlation between the response to blast injury and that to penetrating brain injury. In both cases the same triad of responses occurs. Horsley (1894) noted transient apnea following a side-to-side cerebral injury with a pistol in an animal model. Crockard and colleagues (1977a, 1977b) more recently demonstrated apnea, bradycardia, and hypotension following a controlled cerebral injury that produced a clean wound away from vital structures and major blood vessels in a primate model. Importantly, the apnea, without immediate ventilatory support, led to the death of the animal whereas immediate ventilatory support would lead to a recovery of the animal. More recent studies of penetrating brain injury reproduced this cardiorespiratory response (Carey et al. 1989; Levett et al. 1980), and have suggested that stress waves, propagating through the brain tissue, damage the cardiorespiratory centers at the base of the fourth ventricle. Fissures have been shown in the floor of the fourth ventricle following such penetrating brain injury away from the brain stem that may account for this damage (Sarphie et al. 1999). One conclusion that has been drawn from this parallel is that blast injury may lead to death as a result of the cardiorespiratory response alone, and apnea in particular (Sapsford 2003). It must be stressed, however, that it is not implied that the response to primary thoracic blast injury is mediated via

shock waves transmitted to the brainstem since the apnea and bradycardia induced by blast can be prevented by vagotomy (Ohnishi et al. 2001).

SECONDARY BLAST INJURY

The majority of casualties produced by explosions result from the impact of fragments and debris. In the military environment, the detonation of a high-explosive artillery shell will produce many thousands of metallic fragments of variable mass. Primary fragments, accelerated by the explosive detonation, are classed as either *naturally formed* or *preformed*. Naturally formed fragments arise from the shattering of a solid casing producing, in general, fragments of variable mass and shape. Preformed fragments arise where the case of the device is constructed specifically to control the generation of fragments (such as in grenades and mortars). This results in the production of very small fragments of approximately the same mass and shape, or where the casing contains ball bearings, flechettes, or nails that become primary fragments. In the civilian context the blast-energized debris from explosions, accelerated by the dynamic overpressure, especially in confined spaces, will consist of small and large pieces of glass, splintered wood, plaster, gravel, earth, and any other material that is relatively unfixed. These are secondary fragments.

Close to the device the primary and secondary fragments impact the body at many hundreds of meters per second, easily penetrating body cavities and resulting in a high incidence of serious injuries and death. The wounding power of a missile is dependent on the physical tissue destruction within any given body area or organ and the clinical consequences of the tissue damage within that body area or organ. The anatomical location of the wound is a major factor in the assessment of injury severity.

Among fatalities of terrorist bombings in Northern Ireland between 1969 and 1977, 25% had single or multiple penetrating wounds of the thorax, and the abdomen was penetrated in 26% (Cooper et al. 1983). Penetration of the thorax resulted in a laceration of the major vessels in 18% of fatalities, laceration of the heart in 14%, the lungs in 41%, and the upper respiratory tract in 11%. However, the single most common factors observed in these bomb blast fatalities from penetrating secondary blast injury were penetrating brain injury (66%), skull fracture (51%), and liver laceration (34%).

Interaction between the Response to Blast and Hemorrhage

Blast-injured casualties will often sustain hemorrhage as a consequence of their injuries (Cooper et al. 1983). Hemorrhage initiates a characteristic autonomic response that in turn is modified by the response to injuries such as blast and musculoskeletal injuries.

The pattern of physiological responses to progressive simple hemorrhage (blood loss in the absence of tissue damage and nociception) is biphasic (Barcroft 1944), with an initial tachycardia (due to vagal inhibition and an activation of sympathetic efferent activity) and maintenance of blood pressure via the arterial baroreceptor reflex (Little, Marshall & Kirkman 1989; Secher & Bie 1985). As hemorrhage progresses, and blood loss exceeds 20 to 30% of total blood volume, a depressor phase becomes apparent. This involves a vagally mediated bradycardia (inhibited by atropine; Little et al. 1989), a reduction in peripheral vascular resistance (Barcroft et al. 1944; Evans & Ludbrook 1991) and a marked fall in arterial blood pressure (see Figure 5-13). This second phase is not due to a failure of the baroreflex, since the latter's sensitivity is increased at this stage (Little et al. 1984), nor is it a preterminal event (Hoffman 1972; Sander-Jensen et al. 1986), but rather it is due to the activation of additional reflex(es). The identity of the afferent limb of the depressor reflex is currently uncertain (Kirkman, Shiozaki & Little 1994; Scherrer et al. 1990; Shen et al. 1990), although the cardiac afferent C-fibers may be involved (Evans et al. 2001).

Thoracic blast has been shown to augment the bradycardic, hypotensive response to hemorrhage (see Figure 5-14). Furthermore, the effect of blast on the response to hemorrhage can be attenuated by morphine (Sawdon et al. 2002) (see Figure 5-14). However, the mechanism whereby the depressor response to severe hemorrhage is augmented by the response to blast is unknown. In experimental studies, enhanced blood loss can be discounted as the underlying cause since there was no postmortem evidence of additional blood loss into the body cavities. It is therefore possible that the reflex initiated by exposure to blast modifies one of the reflexes mediating the response to hemorrhage.

Two possibilities are immediately obvious. Either the response to blast inhibits the baroreflex (responsible for the compensatory Phase I of the response to blood loss), or it augments the depressor reflex (responsible for the hypotensive Phase II of the response to hemorrhage). Of these

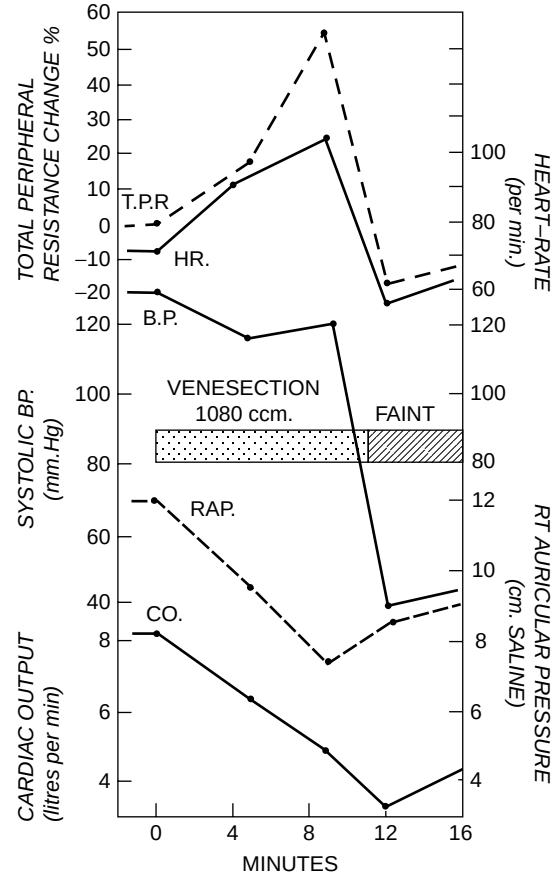


FIGURE 5-13 *Effects of a progressive simple hemorrhage in a male volunteer showing a biphasic response. Blood was withdrawn by venesection until the subject fainted. TPR, total peripheral resistance; Syst BP, systolic arterial blood pressure; CO, cardiac output; Rt auric p; right atrial pressure (central venous pressure). From Barcroft et al. 1944.*

two possibilities the latter appears the most attractive because treatment with morphine (known to block the depressor reflex after simple hemorrhage) also attenuates the bradycardic, hypotensive response to blood loss after blast and uncovers a tachycardic response in its place (Sawdon et al. 2002).

Effects of Blast Injury on the Response to Fluid Resuscitation after Hemorrhage

The effects of blast injury pose special challenges for the resuscitation of hypovolemic casualties. The main early management strategies in hemorrhage are the arrest of bleeding and the replacement of circulating volume.

During the late twentieth century, aggressive fluid administration was encouraged, but this approach was reexamined within military and civilian medical services. Aggressive fluid resuscitation involves the administration of a relatively large amount of fluid as quickly as possible in an attempt to restore and maintain normal arterial blood pressure; the Advanced Trauma Life Support (ATLS) protocol prescribes 2 L of crystalloid solution given intravenously as a bolus, followed by further (variable) aliquots as needed to maintain a normal arterial pressure (Committee on Trauma 2002). In recent years there has been a growing concern that this normalization of blood pressure may lead to clot dislocation and further bleeding (Bickell et al. 1994; Kowalenko et al. 1992; Stern 2001), consequently military and many civilian medical services now practice hypotensive or limited resuscitation to an endpoint of a systolic blood pressure of about 80 mm Hg (a palpable radial pulse in humans) (UK 2006; NHS 2004). However, this approach is not without penalty since prolonged hypotension can result in poor tissue perfusion and ischemic damage (Rafie et al. 2004).

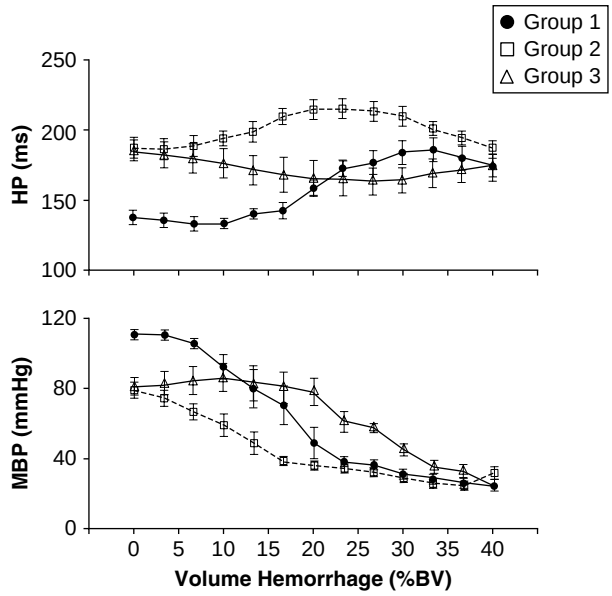


FIGURE 5-14

Effects of a progressive hemorrhage of 40% total estimated blood volume (BV) at a rate of 2% BV.min^{-1} on heart period (HP) and mean arterial blood pressure (MBP) in terminally anesthetized rats 10 min after exposure to thoracic blast (or sham blast) and 5 min after administration of morphine (0.5 mg.kg^{-1}) or vehicle (0.9% saline, 1 ml.kg^{-1}) i.v. Group 1, sham blast, saline; Group 2, thoracic blast, saline; Group 3, thoracic blast, morphine. Data are mean ± s.e.mean. From Sawdon et al. 2002.

In choosing a resuscitation strategy for a hypovolemic blast casualty two conflicting concerns need to be addressed: poor tissue perfusion and oxygen delivery with hypotensive resuscitation versus possible fluid overload and rebleeding with aggressive fluid resuscitation. In casualties who have suffered blast lung, pulmonary oxygen transport will be compromised, leading to some degree of hypoxia. The reduced arterial oxygen content will therefore compound the problems of poor tissue perfusion inherent in hypotensive resuscitation strategies. This is likely to be a particular problem when resuscitation needs to be prolonged. Hypotensive strategies have only been validated in the short term (e.g., 75 min reported by Bickell et al. 1994, in their clinical trial from the time of the emergency call to operative intervention). However, in military practice much longer times have been reported for the evacuation of a battlefield casualty to a surgical

facility for definitive control of the hemorrhage. Recent reports indicate evacuation times of 4 to 5 hours in Afghanistan and 2 to 20 hours in Iraq (Bilski et al. 2003; Bohman et al. 2005) when long distances and operational difficulties are present. In these longer timescales the physiological penalties of poor tissue perfusion arising from hypotensive resuscitation may limit survival. Conversely, the aggressive fluid administration associated with normotensive resuscitation may not be appropriate after thoracic blast injury where cardiac function may be compromised (Harban et al. 2001) since rapid fluid administration could precipitate cardiac failure.

To address the concerns of poor tissue perfusion versus fluid overload, recently a study was completed at Dstl Porton Down, UK, to determine the effects of blast injury on the physiological consequences of hypotensive versus normotensive resuscitation (Parry et al. 2005). The study was conducted on terminally anaesthetized pigs randomly allocated to one of four groups. Animals were exposed to primary blast injury or sham blast. All animals then received a controlled hemorrhage of 30% total estimated blood volume and a five-minute shock phase before being resuscitated to one of two endpoints with 0.9% saline:

- Normotensive, where they were given 2 L/70 kg followed by aliquots to maintain a systolic arterial pressure (SBP) of 110 mmHg
- Hypotensive, where they were given aliquots of saline to restore and maintain SBP at 80 mmHg

The primary focus of the study was survival over an eight-hour period of resuscitation, and secondary measures were indices of physiological compromise such as the development of metabolic acidosis.

Normotensive resuscitation was well tolerated in blast and sham blast groups. However, hypotensive resuscitation was associated with a significantly reduced survival time (see Figure 5-15) in blast-injured animals. The reduction in survival time was clinically significant given current potential evacuation timelines of four hours and greater since approximately 70% of blast-injured animals given normotensive resuscitation survived to the eight-hour end-point of the study, whereas none of those given hypotensive resuscitation after blast survived beyond 3.5 hours after the onset of resuscitation.

The problem with hypotensive resuscitation appeared to be one of poor oxygen delivery to issues leading to a profound metabolic acidosis (see Figure 5-16). Thus, hypotensive resuscitation in the absence of blast injury led to a sustained fall in arterial base excess indicating metabolic acidosis. When blast-injured animals were given hypotensive resuscitation the fall in base excess became profound (see Figure 5-16). By contrast, normotensive resuscitation was associated with a reversal of the shock-induced fall in base excess, even in animals given blast injury (see Figure 5-16).

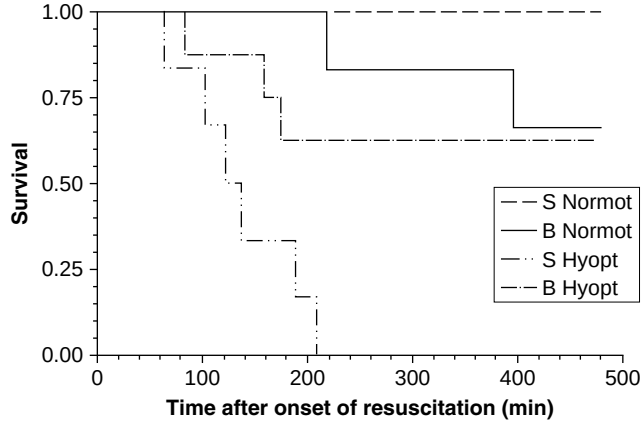


FIGURE 5-15 *Kaplan-Meier survival plot for four groups of animals subjected to either sham blast (S) or blast (B) before a controlled hemorrhage of 30% total estimated blood volume, 5 min shock phase and fluid resuscitation according to either normotensive (ATLS) or hypotensive protocols.*

Therefore it appears that prolonged hypotensive resuscitation may be contraindicated in hypovolemic blast casualties. However, it must be stressed that our physiological study did not address the issue of rebleeding, which is always a concern before surgical control. Consideration, therefore, should be given for the early evacuation of hypovolemic blast-injured casualties to a surgical facility where aggressive fluid resuscitation may be commenced once the risk of rebleeding has been resolved.

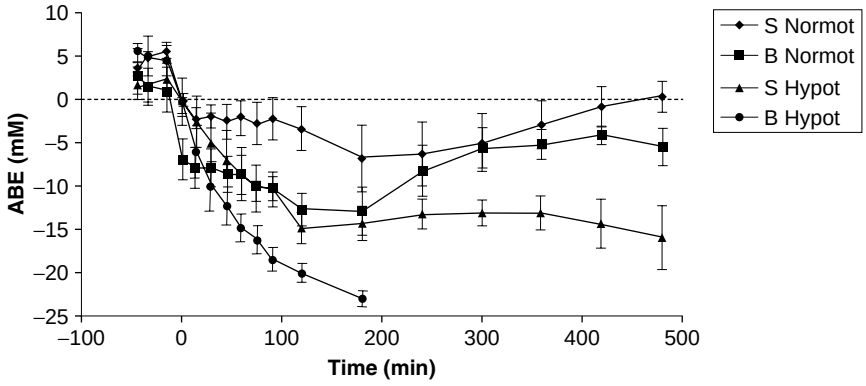


FIGURE 5-16 *Arterial actual base excess (ABE) in four groups of animals subjected to either sham blast (S) or blast (B) before a hemorrhage, shock phase, and fluid resuscitation according to either normotensive (ATLS) or hypotensive protocols. Fluid resuscitation with 0.9% saline in all groups. Time indicates time from onset of resuscitation. First 3 values represent Baseline 1, Baseline 3, and Blast (or Sham Blast). Mean values ± SEM.*

TERTIARY BLAST INJURY

The dynamic overpressure following a blast results in the generation of blast winds of high velocity and increased density of air behind the shock front. This mass movement of air can result in total body disruption, whole body displacement, and collapse of the fabric of a building. Tertiary blast injuries commonly result in blunt injuries often affecting the musculoskeletal system and/or head. Traumatic amputation of limbs is included in this group by most authors (although a component of this aspect of injury, the initial fracture of long bones, is more likely the consequence of the shock wave). Traumatic amputation generally occurs in very severe cases and is rare in survivors of blast injury at a rate of 1 to 2% (Cooper et al. 1983; Hadden et al. 1978; Brismar & Bergenwald 1982; Hull 1992; Pyper & Graham 1983; Rignault & Deligny 1989), but common in immediate fatalities (Hadden et al. 1978; Hill 1979; Waterworth & Carr 1975).

Early Systemic Response to Musculoskeletal Injury

The neural nociceptive barrage initiated by musculoskeletal injury causes profound changes in cardiovascular control resulting in alterations in arterial blood pressure, regional oxygen delivery, and the response to any concomitant hemorrhage, all of which have important implications for morbidity and mortality.

Blood Pressure, Heart Rate and Underlying Neural Mechanisms

Tissue injury/ischemia produces an increase in arterial blood pressure accompanied by a tachycardia (Alam & Smirk 1937, 1938). The increase in arterial blood pressure that accompanies injury is mediated largely by an increase in sympathetic outflow to the vasculature and a consequent increase in total peripheral resistance. This intense sympathetically mediated vasoconstriction induced by injury could lead to a reduction in blood flow to vital organs such as the gut and kidney, and possibly to ischemic damage of these organs (Overman & Wang 1947), hence contributing to the pathophysiology of the response to injury and its sequelae such as multiple organ failure.

The injury-induced pressor response is accompanied by a tachycardia, rather than a bradycardia that would be expected if the baroreflex was functioning normally. This pattern of response is possible because there is a concomitant reduction in the sensitivity and a rightward resetting

(i.e., toward a higher arterial blood pressure) of the baroreflex following injury (Redfern et al. 1984). The reduction in baroreflex sensitivity in man is evident within three hours of injury of moderate severity (e.g., fracture of a long bone), and is persistent such that only partial recovery has occurred at 14 days after injury (Anderson, Little & Irving 1990). This impairment of the baroreflex is accompanied by a persistent tachycardia that is not related to hypovolemia, and a reduction in the variation in heart rate induced by respiration.

The afferent pathway of the response to injury appears to run in somatic (including nociceptive) fibers arising in the damaged tissues. Afferent information then ascends in the spinal cord (probably via the spinothalamic tract) to the brain (Redfern et al. 1984). The precise mechanism of the reduction in the sensitivity of the baroreflex is unknown but the response is reminiscent of the visceral alerting response of the defense reaction (Quest & Gebber 1972) and involves the periaqueductal gray of the midbrain (Jones, Kirkman & Little 1990).

Oxygen Transport

The injury-induced diversion of blood supply away from vital organs has important implications for whole body utilization of the available oxygen delivery (DO_2) and a concept known as critical oxygen delivery. When cardiac output, and hence whole-body DO_2, is progressively reduced (e.g., because of hemorrhage), the body as a whole responds by extracting more oxygen from the available blood flow to maintain oxygen consumption (VO_2). However, this process cannot be extended indefinitely and there comes a point when VO_2 starts to fall as DO_2 is reduced further. This point at which VO_2 becomes dependent on DO_2 is called the *critical oxygen delivery* (DO_{2Crit}) and represents the point at which organs in the body start to suffer physiological damage because of an inadequate DO_2. There is evidence that activation of a neural nociceptive barrage elevates DO_{2Crit} and reduces a patient's ability to extract oxygen from the available blood supply (Kirkman et al. 1995). This increases a patient's susceptibility to problems of reduced oxygen delivery.

The hemodynamic response to muscle ischemia is mediated by central nervous pathways that involve endogenous opioids (Eltrafi, Kirkman & Little 1989; Wyatt, Kirkman & Little 1995). It is therefore likely that opioid-ergic drugs may modify this response. One study has shown that mortality after

blood loss is increased in animals treated with morphine, despite initial maintenance of a higher blood pressure during and immediately after a controlled hemorrhage in animals treated with morphine compared to placebo (Marshall et al. 1998).

Modulation of the Response to Hemorrhage by the Response to Musculoskeletal Injury

It has been known for many years that the response to "simple" hemorrhage (blood loss in the absence of major tissue damage) is biphasic (see Interaction between the Response to Blast and Hemorrhage). The cardiovascular changes elicited by a progressive hemorrhage are markedly attenuated by the presence of concomitant tissue injury (Little et al. 1989). The initial increase in heart rate following a loss of 10 to 15% blood volume is reduced, and the vagal bradycardia following greater losses is prevented. The attenuation of the heart rate changes normally associated with blood loss seems to offer some degree of protection against the hypotensive effects of a severe hemorrhage (Little et al. 1989). However this protection may be more apparent than real, as a lower survival rate has been demonstrated in animals subjected to hemorrhage and concomitant electrical stimulation of the sciatic nerve (to simulate injury) compared to animals subjected to hemorrhage alone (Overman & Wang 1947). It is possible that the better maintenance of blood pressure is achieved at the expense of intense peripheral vasoconstriction leading to ischemic organ damage that will exacerbate the severity of injury. It is tempting to speculate that the splanchnic circulation may be selectively vulnerable to such ischemic damage. There is evidence that when hemorrhage is superimposed on a background of somatic afferent stimulation (to mimic injury) there is a relative redistribution of blood flow from the gut toward skeletal muscle (in contrast to the pattern seen with simple hemorrhage) (Foex et al. 2004; Mackway-Jones et al. 1999). This diversion of blood flow (oxygen delivery) away from metabolically active organs toward relatively inactive resting skeletal muscle may explain the increase in critical oxygen delivery elicited by somatic afferent nerve stimulation (Kirkman et al. 1995) since it effectively wastes a proportion of the cardiac output. Ischemic damage to the intestinal mucosa may lead to an increased intestinal permeability and enhanced translocation of endotoxin (Deitch 1990; Deitch et al. 2001; Wilmore et al. 1988). Therefore the impairment in cardiac function and tissue oxygen delivery associated with blood loss is greater if the

hemorrhage is superimposed on nociceptive nerve stimulation compared to hemorrhage alone (Rady et al. 1991). If the hemorrhage is superimposed on real rather than simulated tissue injury the tolerance to blood loss is reduced even further (Rady et al. 1993).

SUMMARY

Detonation of an explosive generates a shock wave, effectively an instantaneous rise in ambient pressure, which travels outward from the site of the explosion. Fragments and debris are energized both by the explosion and by the mass movement of gas (blast wind) that follows behind the shock wave. Blast injuries are classified according to the biomechanical mechanism of injury. Primary blast injuries are caused by the coupling of the shock wave with the body wall and the generation of stress and to a lesser extent, shear waves within the tissues of the body. The stress wave effects are most pronounced in organs containing interfaces of different densities and therefore the pathology is concentrated in gas containing organ systems such as the lungs. Primary blast injury to the thorax causes a characteristic triad of bradycardia, hypotension, and apnea. This is a reflex response mediated in large part via the autonomic nervous system with an afferent pathway conducted via the vagus nerve. Nitric oxide also is released from the injured lung and this, together with myocardial depression may make significant contribution to the hypotension. The autonomic response to blast is amenable to pharmacological intervention and can be effected by pretreatment with drugs such as those used for protection from nerve agents and pain relief.

Secondary blast injuries are mainly ballistic in nature and result from the impact of fragments of the explosive device's casing and other environmental debris with the body causing largely penetrating injuries that may be associated with life-threatening hemorrhage leading to shock. The response to hemorrhage itself is modified by that to blast and pharmacological treatment. The response to blast also modifies that to subsequent fluid resuscitation after hemorrhage. After blast injury metabolic acidosis develops more rapidly during hypotensive resuscitation and survival time is significantly reduced.

Tertiary injuries are the result of displacement of the body or parts of the body by the dynamic overpressure and subsequent collision with the

ground or other relatively fixed structures. Most of the pathology will be blunt injury and the head and skeletal system are particularly at risk. The response to blunt injuries to the musculoskeletal system also modify autonomic outflow, in this case being characterized by elevation in blood pressure and sympathetic activity, vagal inhibition, and an attenuation of the hypotensive response to blood loss. These changes may worsen ischemia-reperfusion injuries and secondary organ damage.

DISCLAIMER

The views, opinions, and/or findings contained herein are those of the authors and should not be construed as an official position, policy, or decision of the Ministry of Defence.

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CHAPTER 6

Quaternary Blast Injury: Burns

David S. Kauvar, Michael A. Dubick,
Lorne H. Blackbourne, and Steven E. Wolf

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INTRODUCTION

The term *blast injury* refers to the spectrum of injuries resulting from an explosion. These phenomena occur in four distinct varieties. Primary blast injury refers to wounds incurred as the result of blast overpressure. These tend to affect air-containing organs such as the middle ear and lungs and are uncommon, especially among survivors of an explosion. More common are secondary blast injuries, which result from fragmentation of the explosive device or surrounding structures. Tertiary blast injuries result from a casualty's body being thrown or a structure collapsing on him or her. Quaternary blast injury includes burns and inhalation injuries caused

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by the heat or chemical release from an explosion (DePalma et al. 2005). These injuries and their treatment are the subject of this chapter.

Explosions, especially those caused by terrorist bombings, are increasing in frequency around the world (Thompson et al. 2004). These are often high-energy events, with some of the energy released as heat and having the potential to cause burns. Both the incidence and characteristics of the burns seen in explosion casualties are highly variable and both depend on a number of factors specific to the circumstances of the blast itself and to those of the victims at the time of detonation. Burns occurring in explosions frequently coexist with nonburn injuries resulting from the other consequences of blast injury discussed elsewhere in this volume (Baskin & Holcomb 2005). The variable incidence and severity but consistent presence of burns among the injuries seen in the casualties of explosions makes an awareness of blast-related burns important; the combination of blunt and penetrating trauma with burns can result in increased mortality (Hawkins et al. 2005; Santaniello et al. 2004).

The clinical and scientific literature specifically dealing with the subject of burns caused by explosions is quite limited. Most information exists as short passages in chapters on blast injury in larger texts or in isolated published reports of events. In this chapter we use these existing published works along with what is known of the scientific basis of burns to synthesize the epidemiology, pathophysiology, and treatment of explosion-related burns. We describe burn epidemiology by reviewing reports of explosions and resulting burns in both civilian and military situations and further examine the characteristics and pathophysiology, emphasizing those circumstances that influence the injuries produced. We conclude by using this information to provide recommendations and guidelines for the treatment of burns sustained in explosions.

EPIDEMIOLOGY

On October 22, 1981, an explosion occurred at an industrial aerosol plant in Massachusetts, USA. There were 19 casualties treated at local hospitals, all of whom sustained burns (Hull et al. 1985). Between 1975 and 1979, there were a total of 24 terrorist bombings in Jerusalem, Israel. Three hundred and forty of the casualties from these were admitted to a single hospital, with only 4% sustaining burns (Rosenberg et al. 1982).

In addition, as part of a string of terrorist bombings in Paris, the detonation of bombs composed of camping gas bottles resulted in fires, and 33 of 35 victims had burns, with 20 patients requiring care at a burn center (Rignault & Deligny 1988). In general, burns are likely to affect about 10% or fewer of civilians who survive the initial blast in terrorist bombings (Frykberg & Tepas 1988, Kennedy & Johnston 1975). These examples, taken from industrial accidents and terrorist incidents, demonstrate the wide variability of the incidence of explosion-related burns, with some explosions resulting in few or no patients with burns and others causing burns universally.

The severity of burns also varies dramatically from explosion to explosion; of the 12 patients burned in the terrorist bombings just mentioned, the total body surface area (TBSA) burned ranged from 9 to 90% (Rosenberg et al. 1982). These burns span the entire breadth of burn depth as well, with injury ranging from superficial, first-degree burns to full-thickness wounds. Table 6-1 presents a sampling of explosions and their associated burns occurring over the past 30 years around the world. The variability in burn incidence, size, and severity results from differences in the characteristics of the explosions and the individual circumstances of the victims at the time of the explosion. Important general determinants of the presence or absence and the severity of burns resulting from an explosion include whether the detonation occurred indoors or outdoors, the presence of accelerants in the explosion, the victim's distance from the explosion, the presence of clothing or other barriers between the detonation and the victim's skin, and any resulting conflagration of the victim's clothing or surroundings following the explosion.

Factors affecting the severity of quaternary blast injury are as follows:

Increased severity

- Close proximity to explosion
- Indoor explosion
- Unobstructed path from explosion to victim
- Conflagration
- Inability to escape blast area
- Greater weight of explosive material
- Accelerants in or near explosive material
- Bare skin

Table 6-1 A Sampling of Explosions and Their Associated Burns Occurring over the Past 30 Years around the World

Incident	Location	Year	Author	Type	Victims	% Burns	Surface Area	Burn Type	Comments
Tower of London Bombing	London, United Kingdom	1974	Cooper et al.	T	37	27	n/a	Flash	
Public House Bombings (2)	Guildford, United Kingdom	1974	Cooper et al.	T	69	14	n/a	n/a	
Public House Bombings (2)	Birmingham, United Kingdom	1974	Waterworth & Carr	T	21	90	Varied	Flash & flame	Most victims flash burns to exposed areas; clothing on fire caused more extensive, deeper burns
Terrorist Bombings (24)	Jerusalem, Israel	1975–1979	Rosenberg et al.	T	340	4	9 to 90	Mostly flash	Outdoor bombings; clothing on fire caused more extensive, deeper burns
Terrorist Bombing	Bologna, Italy	1980	Brismar & Bergenwald	T	291	26	Half > 30%	n/a	Admitted patients only
Aerosol Plant Explosion	Massachusetts, USA	1981	Hull et al.	I	24	100	20 to 92	Flash and flame	Admitted patients only; clothing on fire caused more extensive, deeper burns
Grain Silo Explosions (2)	Metz & Blaye, France	1982, 1997	Botti et al.	I	22	100	Extensive	Superficial, flash	Autopsy study, no fire noted at scenes
Terrorist Bombings (11)	Paris, France	1985–1986	Rignault & Deligny	T	205	49	Generally limited	Flash	Survivors only; one bomb had accelerant producing 94% incidence of burns
Federal Building Bombing	Oklahoma, USA	1995	Quintana et al.	T	7	57	Varied	n/a	Pediatric patients (ages 2–15); hospitalized survivors only
USS Cole Bombing	Yemen	2000	Davis et al.	T	35	14	Limited	n/a	Survivors only
Terrorist Bombings (10)	Madrid, Spain	2004	Gutierrez de Ceballos et al.	T	243	18	n/a	n/a	Patients treated at a single hospital

Type: T-terrorist; I-industrial; n/a: not available.
Number in parenthesis represents the number of incidences.

Decreased severity

- Increasing distance from explosion
- Outdoor explosion
- Barriers between explosion and victim
- Smaller explosive material weight
- Clothed victim

The morbidity and mortality of blast-related injury varies with the physical environment. For example, mortality is higher when an explosion occurs in a confined space rather than an open area. In a comparative study of bus bombings versus open-air bombings in Israel, the mortality rate for the 204 casualties in open-air bombings was 7.8% whereas that of the 93 bus bombing victims was 49% (Leibovici et al. 1996). In addition to increased mortality, surviving victims from closed area explosions have higher injury severity scores than those in open area detonations. One report places this difference at a mean ISS of 11 versus 6.8 (Singer, Cohen & Stein 2005). As a result of the containment of the fireball and its associated heat (discussed in more detail later) in confined spaces, explosion-related burns would be expected to be more extensive, but data are lacking. In one study that assessed casualties from suicide bombings on buses in Israel, those with burns over 10% of the TBSA had an odds ratio for mortality of 12.9. The same study reported that all 19 casualties who sustained greater than 30% TBSA burns from explosions within a bus died (Almogy et al. 2005). Despite the paucity of data specifically addressing this issue, it is known that indoor blasts result in burns primarily affecting those present in the primary room where the explosion occurred, whereas the threat of burns drops dramatically in secondary rooms (Bean 2004).

Despite the high incidence of explosive injuries in military populations, very little historical information is available on the incidence of burns resulting from explosions in military populations. It is generally presented that burns account for 5 to 20% of combat casualties (Cancio & Pruitt 2003), but the precise incidence of burns resulting from explosions has not been specifically delineated. It is clear that the incidence of burns has varied with the service branch and the specific environment in which the military personnel operate. For example, Champion et al. (2003) reported that in prior conflicts, burns accounted for 2 to 3% of wounds in infantry soldiers, but 25% in armor units and 30% aboard naval vessels (Champion et al. 2003). Burns were observed in up to 47% of U.S. tank crews during

World War II. In more recent conflicts, burns were observed in 26% of Israeli tank crewmen during the Lebanon War, and in the Falkland Island war, the British reported that nearly 100% of the injuries sustained in ship bombings were burns, with about 45% of these considered major burns (Milner & Rylah 1993). In contrast, the terrorist bombing of the USS Cole resulted in only four cases of superficial burns among the 81 injured sailors (Davis et al. 2003). In the first year of Operation Iraqi Freedom, burns accounted for approximately 2% of injuries (Peake 2005); a statistic similar to that observed in Afghan war wounded (Rautio & Paavolainen 1988). Typically burns have been more common in urban operations than in open space fighting (Grau & Jorgensen 1998). As mentioned for the general population, burns also could be just one of several injuries encountered by military personnel in combat, and the incidence of concomitant mechanical trauma in military burn populations is much higher than that seen in civilian populations (Wolf et al. 2006).

Recent military data on explosion-related burns is limited by a lack of information regarding burn casualties who die before reaching medical attention. With this caveat, Operations Iraqi and Enduring Freedom produced over 390 burn casualties from March 2003 to March 2005. All were evacuated to and treated at the United States Army Institute of Surgical Research burn center, which is the only burn referral center for all U.S. military burn casualties. Over 270 of these casualties sustained explosion-related burns. Interestingly, the incidence of primary blast injury sequelae has been extremely low in these patients, with only 14% sustaining rupture of the tympanic membranes, 1% having blast lung injury, and none having primary blast injury to the bowel. Hand burns have been a particular problem, with over 80% of explosion burn patients sustaining injury to the hands. These injuries are frequently quite severe and can be debilitating and have a negative impact on the military mission. The U.S. Army has advocated the expanded use of protective garments, especially gloves, when soldiers are in situations with the threat of explosions.

Burns can account for a significant number of noncombat military explosive injuries as well, and noncombat burns historically have accounted for over half of all burns in wartime (Allen, Whitson & Henjyoji 1970). These may involve the routine burning of waste, mishaps with fuel, as well as accidental munitions detonations. In Operations Iraqi and Enduring Freedom, noncombat related burns accounted for just under half of all

significant burn casualty evacuations (Kauvar et al. 2006). In a study of 742 incidents at munitions depots over a seven-year period, 26.7% of 894 injured soldiers suffered burns (Kopchinski & Lein 2001).

PATHOPHYSIOLOGY

The detonation of an explosive device causes burns through any or all of three mechanisms: momentary flame, radiant heat, and conflagration. These mechanisms are not completely distinct entities, and there is some overlap and influence between them. These will be discussed individually and their relationships outlined in turn.

Momentary Flame

The temperature of the initial flame upon explosive detonation can reach 3,000°C (Boffard & MacFarlane 1993). This intensely hot flame causes burns of varying size and depth and these victims are generally in very close proximity to the detonation, as contact with the flame is necessary to cause burns (Marshall 1977). For example, during a series of bombings in the United States during the 1980s and 1990s, 40% of the victims who opened parcels containing pipe bombs received second- or third-degree burns to the head, neck, trunk, and upper extremities due to their close proximity to the blast (Karmy-Jones et al. 1994). In addition to burns, casualties in such close proximity to a detonation typically suffer multiple serious injuries as a consequence of other effects of the explosion, especially fragmentation injuries. Such multiply-injured casualties have a high chance of dying at the scene, possibly explaining the relative lack of flame burns seen in published reports of explosion victims that were treated or admitted to hospitals.

Burns created by the initial momentary flame increase in depth with increases in the temperature of the initial flame, such as occurs when an accelerant is involved in the explosion. An example of this phenomenon was seen in the 1981 industrial aerosol plant explosion referenced earlier. In this case, flammable isobutane gas acted as an accelerant and there was a correspondingly high rate of full-thickness burns. The victims closest to the blast sustained an average of 85.7% TBSA burns with an average of 56.7% full thickness. As the intensity of the blast is inversely proportional to the square of the distance, victims furthest from the blast had an average burn size of 25% TBSA, with 6.7% being full thickness.

Thirteen of the 14 survivors and all five of the nonsurvivors in this incident sustained full-thickness burns, ranging in size from 9 to 60% TBSA (Hull et al. 1985).

Physical barriers present between the explosion and the victim will serve to decrease the effect of the thermal energy carried by the flame on tissue, and thus the size and depth of the resulting burns. Clothing may also decrease the heat transfer from the initial flame to the skin, but the flame is typically hot enough to ignite textiles other than those designed to be flame-retardant.

Radiant Heat

Victims outside the range of the momentary flame may be burned by the radiant heat generated by the initial flame. These injuries are mostly flash burns of a superficial nature and are typically the most commonly seen burns in victims of explosions. The incidence of flash burns caused by radiant heat varies widely however, from as low as the 4% of burned casualties of the terrorist bombings in Jerusalem referenced earlier to 100% of the dead victims of two grain silo explosions in France in 1982 and 1997 (Botti et al. 2003; Rosenberg et al. 1982). Flash burns can be very serious. For instance, in the terrorist bombing at the Tower of London in 1974, 10 of the 37 victims had flash burns, with five patients requiring hospitalization (Cooper et al. 1983). When death results from flash burns, the skin is noted to become dry, reddish brown in color and parchment-like (Marshall 1977).

The injury created by radiant heat depends on both temperature and the rate at which the energy is applied to the tissues (Cooper et al. 1983). The intensity of thermal radiation increases with the weight of the explosive, with larger amounts of explosive generating greater thermal energy (heat) and therefore deeper burns (Marshall 1977). Radiant heat burns and momentary flame burns are related in that a hotter initial momentary flame, such as occurs with the presence of an accelerant, will radiate greater heat, resulting in deeper burns. Thermal radiation decreases with the square of the distance from the detonation and typically, casualties injured by radiant heat in an explosion are within feet of the explosive at the time of detonation (Marshall 1977).

The rate of heat transfer is dependent on the duration of the explosion, with more rapid explosions generating a higher rate of heat transmission

and thus more severe burns. The effect of the rate of heat transfer in most explosions is likely irrelevant, however, because the influence of the time of heat delivery becomes a factor only if the duration is 10 seconds or more (Cooper et al. 1983). Clothing and other barriers to heat transmission will protect from flash burns caused by radiant heat, and natural textile fibers provide superior protection to synthetic ones, which may melt, resulting in more severe burns. Additionally, light-colored fabrics, which reflect thermal energy, are more protective than dark-colored ones, which absorb heat. Burns caused by radiant heat thus are seen most frequently on unprotected areas such as the face and hands (Marshall 1977). These injuries tend to affect unprotected areas on that portion of the casualty's body facing the explosion. Due to the high rate of energy transfer required to burn skin, flash burns from radiant heat typically are uniform in depth throughout the involved surface area.

It should be mentioned that flash burn injuries may also be associated with inhalation injuries resulting primarily from the release and inhalation of toxic gases of combustible materials (Boffard & MacFarlane 1993). In ongoing U.S. military operations, the current rate of inhalation injury (diagnosed by fiber-optic bronchoscopy of the upper airways) in casualties of explosions resulting from hostile action is 13% percent (Kauvar et al. 2007). The incidence of inhalation injury in the military burn population is higher than that seen in the civilian burn population, and the incidence is particularly high among casualties burned in combat operations (Wolf et al., in press).

Conflagration

The third mechanism of blast-induced burns occurs when an explosion causes a fire involving the victim's clothing or surroundings. Both the momentary flame and the radiant heat of an explosion can lead to fires, especially if the explosion involves an easily combustible material (Marshall 1977). As the temperature of the initial flame and thus the radiated heat increases, as is seen with the use of accelerants and larger amounts of explosive material, the likelihood that an explosion will result in a fire increases. Whereas momentary flame and radiant heat burns affect victims within feet of an explosion, the resulting conflagration can affect victims further away from the detonation if their surroundings catch fire. The specific circumstances of victims and their surroundings following the explosion will determine the severity of burns from the conflagration.

The severity of burns caused by conflagration relates to the heat of the fire and to the duration that tissues are exposed to this heat. Victims who are trapped and unable to escape an area that is on fire will sustain more severe burns than those who can escape rapidly because they will be exposed to fire for a longer period. The surface area burned by the conflagration following an explosion relates to the amount of tissue exposed to the fire. As might be expected, the extent of flame burn-induced injury will be greater if the force of the blast itself rips off or ignites clothing. This was observed in burns of the 19 of 21 deaths that occurred from terrorist explosions set off in crowded pubs in Birmingham, England (Waterworth & Carr 1975). As the typically unprotected head and hands constitute about 20% of the body surface area, it could be implied that burns over 20% involve clothes that caught on fire or clothes blown away by the blast (Cooper et al. 1983). If the clothes do not catch fire, then the affected areas will consist primarily of exposed portions of the body such as the face and hands. If the clothing does catch fire, however, and the victim is unable to put out the flames rapidly, then severe, large surface area burns will ensue as the clothing burns against the skin.

TREATMENT

The treatment of explosion casualties with burns should be undertaken with the understanding that many if not most of these victims will have associated nonburn injuries and that the combination of these with burns can increase mortality above and beyond that seen with blunt and penetrating trauma alone (Hawkins et al. 2005; Santaniello et al. 2004). Though true primary blast injury is very rare, many explosion casualties sustain serious fragmentation injuries in addition to burns. Although any trauma center should be able to manage the blunt and penetrating trauma caused by primary, secondary, and tertiary blast injury, only a burn center will have the facilities and expertise to specifically manage severe burns over the long course of treatment and rehabilitation that typically is required. Only coordinated burn care can reliably reduce the potential for added complications, morbidity, and mortality brought on by concomitant thermal and mechanical trauma. For this reason, the standard burn center transfer criteria espoused by the American Burn Association should be used to determine the appropriate setting for the definitive care of burn-injured blast casualties. In this section, we will discuss the treatment of the burns

associated with blast injuries in two phases: field care (including initial triage, treatment, and evacuation) and definitive care at the burn center.

The American Burn Association Burn Center's transfer criteria include:

- Partial thickness burns to greater than 10% of the total body surface area in patients under 10 years or over 50 years of age (20% between age 10 and 50)
- Burns that involve the face, hands, feet, genitalia, perineum, or major joints
- Third degree burns in any age group
- Electrical burns, including lightning injury
- Significant chemical burns
- Inhalation injury
- Children with any of the preceding burn injuries
- Burn injury in patients with preexisting medical disorders that could complicate management
- Any patients with traumatic injury (such as fractures) in which the burn injury poses the greatest risk of morbidity or mortality; if the trauma poses the greater immediate risk, the patient must be initially stabilized in the nearest appropriate facility before being transferred to a burn unit
- Any burned children if the hospital initially receiving the patient does not have qualified personnel or equipment for children

Field Care

An explosion is likely to produce many injured patients, resulting in a mass-casualty situation. Such a situation exists when the number of injured patients exceeds the field care system's ability to provide standard care to all patients simultaneously. Under these circumstances, field triage must be initiated, and patients sorted and prioritized for evacuation based on the severity of their injuries and the likelihood of their survival. Those patients with the most severe but survivable injuries are given the highest priority for evacuation, and those who are unlikely to survive even with prompt evacuation are assigned the lowest priority. Although easily overlooked in the initial evaluation of a patient with multiple blunt and penetrating injuries, a patient's burns should be included in their triage assessment and the criteria listed earlier should be used to determine the type of center to which a patient should be evacuated.

The initial management of burns is guided by the principles set forth in the Advanced Burn Life Support program, promulgated by the American Burn Association. A significant initial aspect of the field care of burns is to stop the burning process by moving the patient out of burning surroundings and by the removal of burning clothing. Stopping the burning process should be accomplished without actively cooling or wetting the patient, however, because hypothermia contributes to coagulopathy and complicates the treatment of coexisting injuries. Though burns themselves may not be rapidly fatal, a patient with a large surface area burn (typically >20% TBSA) will require the prompt initiation of intravenous fluid resuscitation to avoid the rapid onset of burn shock through intravascular fluid losses from burned tissue and capillary leak resulting from systemic inflammation, seen especially when inhalation injury is present. In patients with large burns, intravenous resuscitation with warmed Ringer's lactate should be initiated in the field, especially if evacuation to a burn center will be delayed. Patients with burns of 20% or greater of the TBSA should be prophylactically intubated due to the likelihood of the development of total body and pulmonary edema from large-volume resuscitation. The burn wounds themselves do not require specialized field treatment other than the application of dry dressings directly over burned areas. Warm, dry sheets and/or blankets should be placed over burned patients to help them conserve heat and prevent further contamination of the burn wound. Burns to the face may result in airway obstruction through tissue edema or may be a clue to the presence of inhalation injury. Facial burns are common in patients with explosion-related burns, and patients with them should be managed with a definitive airway (i.e., endotracheal intubation).

Burn Center Care

Upon arrival at a burn center, the victim of blast injury should be treated like any trauma victim, according to the principles set forth by the American College of Surgeons Committee on Trauma's Advanced Trauma Life Support curriculum (2004). An evaluation of the patient's airway, breathing, and circulation provides an initial estimate of their vital functions. A rapid assessment of the patient follows, with the purpose of identifying and rapidly addressing life-threatening injuries. Intravenous fluid resuscitation, if not already initiated, should be started at this point. In the very early phases of care, resuscitation will be guided by standard

hemodynamic parameters such as heart rate and blood pressure. Then, the formulas outlined next are used to estimate hourly fluid requirements with the dual goals of providing adequate circulating volume while avoiding the complications of over-resuscitation. A comprehensive, head-to-toe examination, including radiographs and invasive monitoring, is undertaken, with the intent to discover occult injuries. It is during this phase that an initial estimate of burn size is made and the decision of whether to admit the patient to a burn intensive care unit or standard ward is made. It is important to identify all injuries early in the admission, because some burns will require urgent therapy including operative intervention, and coordination of care with physicians treating other injuries, such as fractures requiring early operative therapy, will be a priority.

Historically, military burn casualties have been severely injured, as seen during a nine-year period of the Soviet Union's interventions in Afghanistan, when 42.6% of burn wound victims required intensive care unit care independent of the cause of the burn (Grau & Jorgensen 1998). Upon arrival to the burn ward or intensive care unit, the patient is showered, and the burn wounds cleaned. A comprehensive assessment of the size and depth of the burns is made using the technique of Lund and Browder (1944). Due to the nature of blast-related burn injury, many patients will have superficial burns, and many will be small in size. Even small or superficial burns can produce complications in the care of other injuries. These burns can be a source of sepsis if not treated properly with topical antimicrobial therapy and appropriate burn coverage. Attention to associated nonburn injuries should be given, and appropriate therapies initiated. Many patients with severe burns will have been close to the detonation, and these patients will likely have some of the most severe injuries. Appropriate treatment of these patients will require intensive coordination between multiple clinical services to provide the best chance for a good outcome.

Standard care for burns should then be undertaken. A thorough review of such care is beyond the scope of this chapter, but certain principles are worthy of mention. Burn resuscitation should be guided initially by the Brooke or Parkland formulas, with 2 or 4 mL/Kg/percent TBSA burned of Ringer's lactate given in the first 24 postburn hours. Half of this is given in the first eight hours, and the rest over the ensuing 16 hours. Once resuscitation and monitoring at the burn center have begun, however, ongoing

resuscitation should be guided by end-organ perfusion, with fluid administration titrated hourly to maintain a urine output of 0.5 mL/Kg/hour.

Patients with full-thickness burns have been demonstrated to benefit from early operative excision and grafting of their burn wounds (Cope et al. 1947; Gray et al. 1982; Herndon & Parks 1986; Janzekovic 1970; Wu et al. 2002). This technique, whereby definitive burn coverage is achieved within 48 hours, can reduce the incidence of burn sepsis and wound infection, and improve overall burn outcomes. Partial-thickness injuries should be covered by a skin substitute (e.g., Biobrane®, UDL Laboratories, Inc, Rockford, IL) or treated with topical antimicrobial agents as soon as possible following admission.

The identification and treatment of inhalation injury is another important aspect of burn care relevant to blast-related burns. Pulmonary complications in blast casualties may be influenced by thermal inhalation injury, and all patients in whom there is a suspicion of inhalation injury should undergo bronchoscopy for diagnosis. The diagnosis is confirmed with a plausible history and bronchoscopic verification of airway edema, erythema, and epithelial sloughing. If found, inhalation injury should be treated expectantly with ventilator support until airway edema resolves. Prompt and aggressive pulmonary toilet, including in some cases inhaled heparin, is also a vital part of the management of inhalation injury.

Burns, especially those to the hands and face, require intensive rehabilitative care, specialized to the treatment of burns. This care can be complicated by the fact that many burn casualties injured in explosions will have other injuries requiring rehabilitative care, primarily orthopedic and head injuries. These may impair a patient's ability to participate in the intensive burn rehabilitation necessary for optimal long-term outcomes. Burns sustained in military combat-related explosions can have a significant impact on mission readiness. In recent U.S. military experience, fewer than 40% of burn casualties from such explosions have been able to return to duty without limitations (Kauvar, et al. 2007).

CONCLUSION

From this discussion, it would appear that among survivors of terrorist bombings against civilian targets, the incidence of burns is relatively infrequent. As shown in the recent Madrid train bombings, most of the burns

tend to be mild flash burns with correspondingly low mortality (Gutierrez de Ceballos et al. 2005) unless the blast is concentrated in a confined space. The incidence and severity of burns will generally increase if the blast results in a fire or is powerful and hot enough to ignite or blow away clothing. Burns, though not as frequent as mechanical trauma in blast mechanisms of injury, can be significant contributors to patient morbidity in both civilian and military populations. The ability to provide adequate burn care from the point of wounding through the burn center and rehabilitation care phases is vital to preparing to deal with the injuries that result from explosions.

DISCLAIMER

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official nor do they reflect the views of the Department of the Army or the Department of Defense.

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PART 3

Modeling and Mechanisms of Primary Blast Injury

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CHAPTER 7

Multiscale Computational Modeling of Lung Blast Injuries

Andrzej Przekwas

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Summary and Conclusions

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INTRODUCTION

Understanding Blast Wave Injuries

In recent years, explosive devices have become the preferred weapon in the majority of terrorist attacks in war zones and other regions of political conflict worldwide. Relative ease of manufacturing and portability of Improvised Explosive Devices (IEDs) make them the weapon of choice in terrorist and insurgent activities. Today in Iraq, civilians and security personnel sustain blast injuries during terrorist attacks, which often involve explosive loaded suicide actions, roadside bombs, car bombs, or package bombs. A recent report by Murray et al. (2005) documented that 78% of military personnel wounded in action and treated at a medical unit in Iraq had been injured by explosive devices. With improved protective body armor and better combat zone medical treatment, military casualties are able to survive even larger blast explosion incidents, though often returning from war zones with multiple severe injuries in often unpredictable patterns (Scott et al. 2006). Explosions have the potential to inflict many different types of injuries on victims, including blunt and penetrating trauma, amputations of body extremities, as well as pressure wave injuries (Wightman & Gladish 2001; Gawande 2004; DePalma et al. 2005).

During recent meetings at DARPA, TSWG, DoD Medical Labs, and at VA facilities, representatives of military doctors and medics, military and civilian medical scientists, and DoD decision makers emphasized the importance of basic research in trauma injury mechanisms, personnel protection, and treatment planning. It also recognized that better understanding of explosion blast injury mechanisms will help design better protective armor and improve medical care. Advanced experimental and theoretical research can help the medical community to develop better diagnostics and medical training, optimize the resuscitation and pharmacological/interventional treatment planning, and provide more intelligent forensics and logistical support. The urgency and need for a better understanding of blast injury is exemplified by the following statement in the CDC document, *Explosions and Blast Injuries—A Primer for Clinicians 2003*: "As the risk of terrorist attacks increases in the U.S., disaster response personnel must understand the unique pathophysiology of injuries associated with explosions and must be prepared to assess and treat the people injured by them" (http://www.bt.cdc.gov/masscasualties/explosions.asp).

New experimental and computational methods are necessary to understand how the blast wave penetrates the human body, how it interacts with brain tissue and air-filled organs, the physiological events involved in the injury formation, the most effective resuscitation and therapeutic treatment procedures, and most importantly, how to design personal protection armor countermeasures to prevent major injury. Previous explosion and blast wave trauma injury research was almost exclusively conducted on cadavers and on animal and physical "models" (Cooper 1996; Argyros 1997; Mayorga 1997; Januszkiewicz, Mundie & Dodd 1997). Sensor instrumented dummies constructed to represent human anatomy with approximations for human organs have been used to study bomb blasts and car crashes. Small and large animals such as rats and pigs also have been used to study blast injury to the lungs, brain, and other organs. Unfortunately, physical surrogates constructed of synthetic materials or cadavers are not biofidelic, and beyond providing mechanical reaction forces, they cannot provide important physiological responses to blast loads. Animal models are anatomically vastly different from humans, yet they can provide insights into trauma pathophysiology and potential treatment, but their responses are often dissimilar to humans and scaling animal-to-human results is challenging and often questionable. However, both physical and animal models can provide benchmark quality biomechanical and physiological data for calibration and validation of advanced, physiology-based computational models of human body biomechanics and trauma injury.

Computational modeling of blast injury and resulting trauma is extremely difficult as it involves a range of disciplines (gas dynamics, structures dynamics, biomechanics, physiology, pathology, biology, biochemistry), time scales (microseconds to days), and space scales (microns-size alveoli to meters-scale human body and distance from blast). Several approaches have been used to study blast injuries and design body armor (Cooper 1991, Markis & Nerenberg 2000; Vaziri & Hutchinson 2006). Earlier models used theoretical and semiempirical correlations to relate the blast shock wave parameters to severity of injury. One of the first fundamental injury biomechanics models was proposed by Stuhmiller et al. (1988) by correlating the extent of injury to the amount of irreversible energy loss in a mass-spring-damper system. This method has provided a theoretical basis for current injury models such as the U.S. Army MRMC INJURY 8.1 model (http://www.momrp.org/). The same team also developed the first Finite Element Method- (FEM) based approach for modeling a sheep's thoraco-abdominal response to blast

waves (Chuong & Stuhmiller 1985). Since then, several reduced models and FEM-based blast injury models have been reported (Viano & Lau 1988; Stuhmiller et al. 1999). The state of the art in mathematical modeling was reviewed by Stuhmiller et al. (1999). More recent thoracic injury modeling work has been presented by various authors in the context of blast injury (Przekwas et al. 2004; Friend 2005; Imielinska, Przekwas & Tan 2006), ballistic nonpenetrating impact and resultant behind armor blunt trauma (BABT) (Grimal, Naili & Watzky 2005; Roberts et al. 2006), and automotive crash analysis (Wang 1995; Lizee et al. 1998; Ruan et al. 2003; Forbes 2005). In the last few years there has been significant interest in the development of whole body anatomical models for FEM-based crash biomechanics study in automotive accidents. In 2002, Iwamoto et al. presented a Total Human Model for Safety (THUMS) finite element model of the human body that was developed by the Toyota Central R&D Lab and has been used by several users. To the best of our knowledge, such a model has not been developed for military applications, despite great need and potential. This chapter presents a discussion of the overall approach for multiscale modeling of blast wave human body injury as well as a description of key model components.

Blast Wave Dynamics and Forces

An explosion is caused by the rapid exothermic oxidation of a solid or liquid material into gaseous reaction products resulting in a large energy release in the form of increased pressure and temperature within the explosive compound. That reaction and pressurization propagation process within the explosive is known as the *detonation wave*. In solids and liquids, detonation waves propagate from the center of ignition outward at supersonic speeds of 6 to 8 km/s (6.8 km/s for TNT) (Henrych 1979), whereas in gases detonation waves move at 1 to 3.5 km/s. For comparison, the speed of sound in air in normal atmospheric conditions is 340 m/sec and in freshwater is 1435 m/sec. The ratio of the wave speed, u, to the sound speed, c, is known as the *Mach number*, Ma = u/c. Blast waves propagate at *supersonic* speeds, Ma >1. The explosion reaction typically is completed within a few microseconds, converting the originally solid material into a highly pressurized gas. Typical explosives, such as C4, generate pressures of thousands of atmospheres (1 atm = 101,325 N/m^2; or Pascals) and temperatures of 2,000 to 4,000 K. These reaction gases expand violently, compressing and forcing out the surrounding air. A pressure wave, *blast wave*, is formed, spreading in air radially outward. The blast

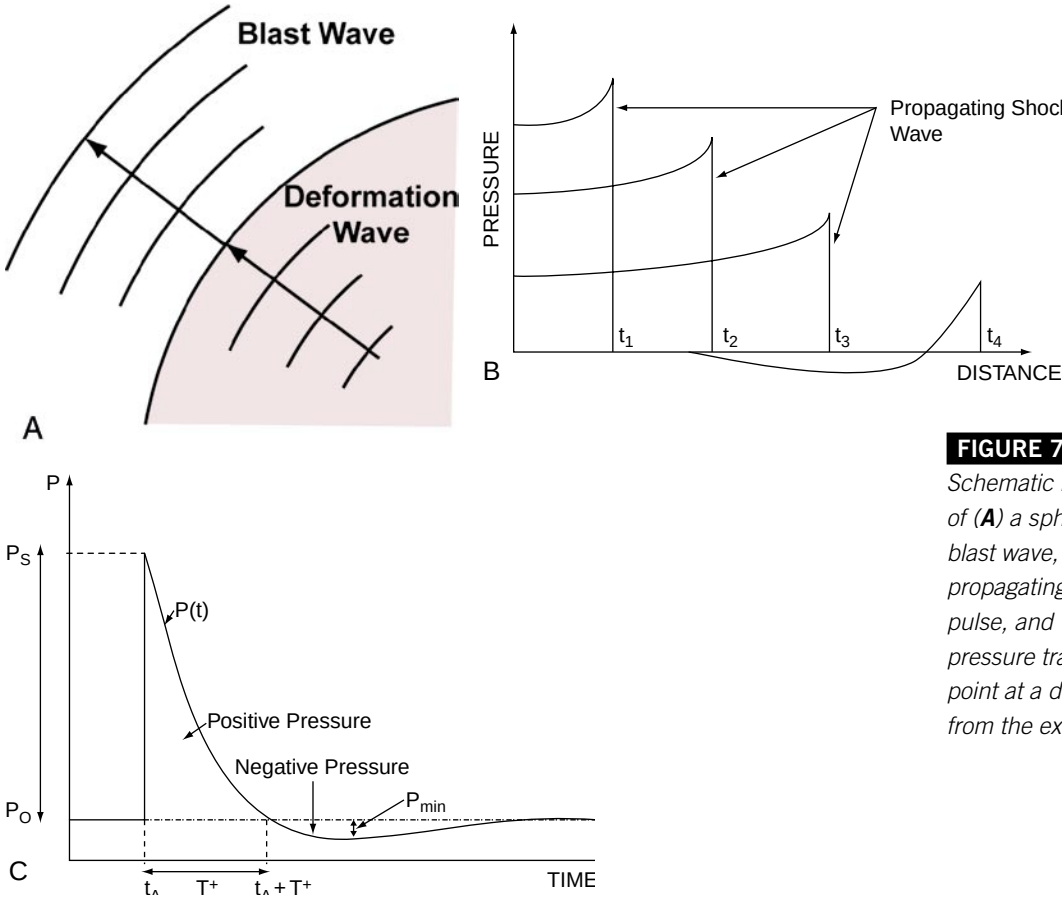

FIGURE 7-1
*Schematic illustration of (**A**) a spherical blast wave, (**B**) propagating pressure pulse, and (**C**) a pressure trace at a point at a distance from the explosion.*

wave consists of a microns-thin pressure wave, known as the *shock wave*, followed closely by the blast wind. There is a dramatic increase in pressure across the shock wave. Part of the explosive (chemical) energy is used to break up the munition casing, resulting in the generation of fragments, which are accelerated by the blast wind. These kinetic projectiles also move radially outward, but at speeds much slower than the shock wave. Figure 7-1A schematically presents the spherical propagation of the detonation and blast waves, and Figure 7-1B shows the pressure profile as a function of the radial distance from the explosion center at selected times. Note in Figure 7-1B that as the gases continue to expand, the pressure drops, creating a relative vacuum at t = t4 behind the shock wave.

Based on the Sedov–Taylor blast wave self-similar solution (Taylor 1950), the pressure-time history of a spherical blast wave can be expressed in the form of the Friedlander equation (Baker 1973; Kinney & Graham 1985; Sedov 1993):

$$p(t) = p_0 + p_S\left[1 - \frac{(t - t_a)}{T_S}\right] \cdot \exp\left[-b\frac{(t - t_a)}{T_S}\right] \tag{7.1}$$

where t is the time measured from the instant the shock wave arrives, p_o is the ambient pressure, p_s is the peak overpressure, T_s is the duration of the positive phase, t_a is the arrival time, and b is a positive constant called the waveform parameter that depends on the peak overpressure. P_{min} is the minimum pressure reached. Figure 7-1C shows the pressure profile generated by an ideal blast wave at a point away from the center of the explosion. Before the shock wave reaches the given point, the pressure is equal to the *ambient pressure* p_0. At arrival time t_a, the pressure rises discontinuously to the peak value of $p_0 + p_s$. The pressure then decays to ambient pressure p_0 in total time $t_a + T$ (*positive phase*), drops to a partial vacuum pressure of value $p_0 - p_{min}$ (*negative phase*) due to the overexpansion of gases, and eventually returns to the ambient pressure p_0.

It is possible to calculate the peak overpressure as a function of the explosive charge weight and the distance from the explosive charge by introducing the so-called scaled distance Z,

$$Z = \frac{R}{W^{1/3}} \tag{7.2}$$

where W is the charge mass expressed in kilograms of "equivalent" TNT and the distance R from an explosive charge. The use of Z allows a compact and efficient representation of blast wave data for a wide range of situations. For example, if a given overpressure is felt at radius R_1 for an explosive mass W_1, a second explosive with equivalent mass W_2 will generate the same overpressure at radius R_2 as given by the following relation:

$$\frac{R_1}{R_2} = \left(\frac{W_1}{W_2}\right)^{1/3} \tag{7.3}$$

There are several sets of equations for predicting peak static overpressure, $p_S \sim Z$, developed using both numerical and experimental techniques. The best known semiempirical models are the Brode and Henrych equations (Brode 1955; Henrych 1979; Smith & Hetherington 1994). Brode (1955) proposed two equations for near and far field. The Henrych model, which is more accurate in the near zone, divides the analysis into a near, middle, and far field zones and expresses the p_S (in kPa) as:

$$p_S = \frac{1407.2}{Z} + \frac{554.0}{Z^2} - \frac{35.7}{Z^3} + \frac{0.625}{Z^4} \qquad 0.05 \le Z \le 0.3 \qquad (7.4)$$

$$p_S = \frac{619.4}{Z} - \frac{32.6}{Z^2} + \frac{213.2}{Z^3} \qquad 0.3 \le Z \le 1.0 \qquad (7.5)$$

$$p_S = \frac{66.2}{Z} + \frac{405.0}{Z^2} - \frac{328.8}{Z^3} \qquad 1.0 \le Z \le 10.0 \qquad (7.6)$$

Equations (7.4–7.6) and (7.1) provide a first approximation theoretical model to calculate the pressures and forces (pressure area product) of an explosion blast wave impacting an object. In real conditions blast waves interact with the ground, walls, and other objects, and the blast wave loading dynamics on a given object (e.g., human body) are greatly affected by these reflected and diffracted waves. Some of these phenomena are discussed next.

Blast Wave Interaction with Objects and the Human Body

When a blast wave encounters an object of higher density, such as ground or a human body, it will both reflect off the object and diffract around it. The reflected wave travels back toward the origin and the overpressure of the reflected wave may exceed the overpressure of the incident wave. The magnitude of the reflected pressure is related to both the angle of incidence of the blast wave and to the incident shock strength. The incident wave will also penetrate the object and generate compression and shear stress waves within the object. The exact behavior depends upon the geometry of the object, the angle of incidence, and the power of the wave. When explosions occur indoors or in street canyons, standing waves and enhanced differences in pressure occur because of the additive effects of reflections from walls and rigid objects (Liang, Wang & Chen 2002). Figure 7-2A presents a schematic of an incident shock wave interacting with a body, illustrating the propagating shock wave, shock reflection and diffraction, and stress wave transmitted through the body.

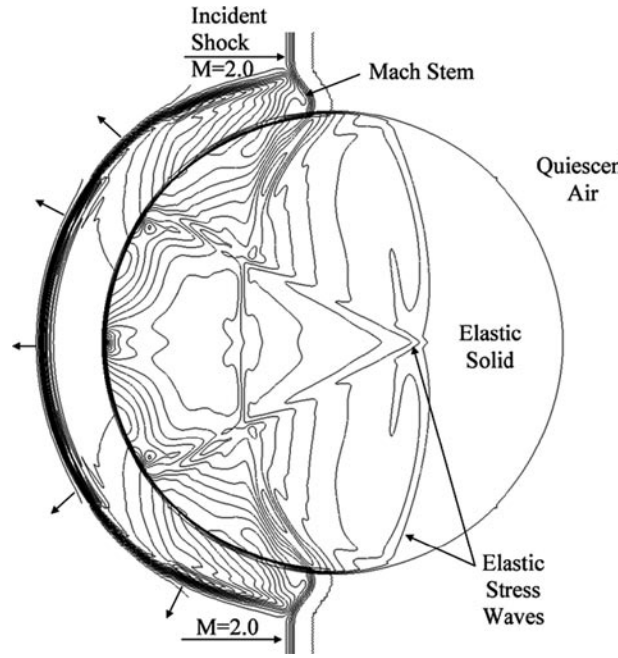

FIGURE 7-2
An example CFD simulations of a planar shock wave diffracting over an elastic cylinder showing pressure contours at a time instant when shock has just passed over the body.

In this case, the sound speed in the elastic solid is larger than the shock wave speed in the air and the elastic stress waves inside the body, shown in Figure 7-2, propagate ahead of the shock wave. Shown are the pressure field and the shock wave pattern, including the incident wave, reflected wave, and diffracted waves (Mach stem) around the body, at a time instant when the shock wave passes across the center of the body.

Shock wave reflections from objects can be either normal, when the wall-shock normals are at zero angle, or oblique, when the angle of incidence is small, less than about 40° in air. When a blast wave strikes an object it will generate a pressure on the surface of the object that is greater than the peak static pressure of the wave. Intuitively this can be explained by the fact that the forward moving air molecules are stopped at the wall while the molecules behind will still compress the ones on the stopped wave front. Mathematically it can be expressed that, for the normal reflection of an ideal gas from a rigid wall, the total pressure on the object wall (the peak reflected pressure, p_r) is the sum of the static pressure, p_S, and the dynamic pressure $q = \rho v^2/2$:

$$p_r = 2p_s + (\gamma - 1)q \tag{7.7}$$

where γ is the ratio of specific heats ($\gamma = 1.4$ for ideal gas). Using Rankine-Hugoniot relations (Baker 1974; Smith & Hetherington 1994) relating mass, momentum, and energy of the incoming wave before the impact and at the wave reflection instant one can eliminate q and relate the reflected pressure to the peak overpressure and the ambient pressure:

$$p_r = 2p_s((7p_0 + 4p_S)/(7p_0 + p_S)) \tag{7.8}$$

For an object such as a human body, the blast wave reflected pressure (p_r) load on the front (proximal) side for a short period of time will be much larger than the peak overpressure, p_S. The side walls, parallel to the shock propagation direction, will be loaded as the wave passes over them with the p_S. Therefore, the time for loading can be calculated from the blast wave velocity. The rear side loading begins after the blast wave passes the object and after the diffractive waves meet at the center back side. In addition to the pressure loading, the object will also experience friction drag forces, F_D, induced by the blast wind:

$$F_D = C_D \cdot q(t) \cdot A \tag{7.9}$$

where $q(t)$ is the dynamic pressure ($q = \rho v(t)^2/2$) of the wind, A is the friction wall area loaded, and C_D is the drag coefficient of the object, which depends on its shape. The drag force will appear after the pressure force and its duration will be longer. Therefore, the total transverse force on an object is a sum of the forces caused by the reflected pressure and drag force.

This cursory analysis of shock wave patterns and the reflected pressure levels, p_r, indicate that blast waves are far more lethal near reflecting surfaces. A person next to a solid wall will be exposed to not only the forward shock wave but also to even stronger reflected waves. Blast injuries in a confined space is particularly severe as the person is exposed to multiple reflected waves coming from various directions. This is demonstrated on a computational example in the next section. Blast loads on large rigid objects will create strong crushing forces but cause little or no object translocation. Smaller objects, such as explosive casing, debris, and even human beings, will be propelled in the air by pressure and blast wind loading. The translational force will last for a brief time but the drag loading will have a longer duration and can lead to significant body translocation in addition to the overpressure damage.

When a shock wave impacts the living body, a series of instantaneous physical events take place. The body is affected by the primary incident wave, by the wave reflected at the body surface and by the diffracted waves on the side and at the back of the body. From the human injury viewpoint, the most important part of the wave energy is the one that is transmitted into the body in the form of both positive (compression) and negative (tension) stress waves as well as shear stress waves. Normal stress can be defined as the perpendicular force per unit area applied to an object, in a way that compresses (compressive stress) or stretches (tensile stress) the object. Shear stress, or simply shear, is similar to stress, except that the force is applied such that the material is sheared or twisted. Note that the pressure entering the tissue may be higher than in the primary wave, due to a damming up of pressure against the body surface. In air, high frequency acoustic waves and shock waves are decaying due to viscous dissipation, producing heat. In tissues, the steep gradient pressure waves will also be absorbed by viscoelastic damping and tissue plastic deformation (tearing, breaking), resulting in mechanical injury. When the pressure wave crosses material interfaces with different densities, large perturba-

tions in stress and deformation take place. A wave impacting denser material will compress it, creating larger stress (pressure), and when it emerges from denser to lighter material it will create large deformations. Therefore in the human body, organs and tissues of different densities are accelerated at different relative rates, resulting in displacement, stretching, and shearing forces. For those reasons the most vulnerable parts of the body are the air- and gas-containing organs, such as the ear drums, lungs, and intestine. In spite of relatively uniform density and protective barriers, including the scalp, skull, meninges, and subarachnid cerebrospinal fluid, the brain is also susceptible to blast wave injuries. Highly anisotropic material properties in the brain and immense vascular perfusion will result in nonuniform absorption of the wave energy, stretching and breaking neural axons and the capillary blood brain barrier. Other homogeneous solid viscera transmit the pressure wave to the distal side of the body and are much less susceptible to blast wave injury. In general, the risk of injury is related to the blast energy delivered to the body and absorption by various tissues.

Free-standing objects exposed to the blast wave (shock wave and the blast wind) will also be displaced. The time integral of the total pressure ($p + \frac{1}{2}v^2$) and the viscous drag loads integrated over the entire surface of the object will result in a net force and moment causing object translation and rotation in space. The extent of the movement depends on the object mass (inertia), and the magnitude of the total force and moment, according to Newton's law (discussed in the next section). Typically solid objects such as shrapnel, debris, and human bodies will experience translational motion after the shock has already passed. The time delay depends on the inertia of the body. Current explosive devices often are loaded with metallic objects, which are accelerated by the detonation and blast waves, to inflict penetrating injuries in addition to the blast wave.

Based on this physical description of the blast wave events, explosions have the potential to inflict three injury types: *primary blast injury (PBI)* due to the shock wave, *secondary* injuries due to blast-propelled debris fragments causing blunt or penetrating ballistic trauma, and *tertiary* injuries due to human body translocation by blast loads and the resulting impact on rigid objects, thus resulting in blunt force trauma. *Quaternary* injury often refers to all other types of injury including burns, environmental wound contamination, among others. Detailed discussion of the injury mechanisms and pathophysiology of trauma for these injury types,

particularly lung injury, have been described in military medicine publications and reports (Stuhmiller et al. 1996; Argyros 1997; Elsayed 1997; Januszkiewicz et al. 1997; Mayorga 1997; Wightman & Gladish 2001; Avidan et al. 2005; DePalma et al. 2005; Scott et al. 2006) and are discussed in more detail in other chapters in this book. The remaining sections of this chapter focus on mathematical modeling of physical, biomechanical, and physiological phenomena during blast wave interaction with the human body and human organs, with emphasis on the lungs.

MULTIPHYSICS, AND MULTISCALE APPROACHES IN MODELING BLAST INJURY

Modeling Approaches

Mathematical modeling of human body traumatic injury has been investigated since the mid-1970s, first using approximate (reduced) models derived either from fundamental mechanics or from curve fitted experimental data, and more recently using high-fidelity computational models. Unlike the reduced models, which typically involve a single discipline, the most recent high fidelity models are truly multidisciplinary. The development of high fidelity human body impact injury models has been driven by automotive safety regulations and competitive and innovative car design. With few exceptions, blast injury research was almost exclusively empirical. Initial interest in blast injury modeling was investigated in the United Kingdom and Canada to help design safe demining suits (Cooper 1991; Markis & Nerenberg 2000). Until very recently, military interest in modeling human injury was focused exclusively on ballistic injury protection, as was design of military personnel protective armor. High fidelity human injury models, pioneered by Stuhmiller et al. (1996, 1999), recently have been improved in terms of resolution (Grimal et al. 2005; Roberts et al. 2006; Niu, Shen & Stuhmiller 2007; Aare & Kleiven 2007) and extended from the biomechanics discipline alone, to multiphysics modeling involving blast gas dynamics, biomechanics, and physiology (Przekwas et al. 2004; Friend 2005; Ding et al. 2005; Imielinska et al. 2006). The recent explosion in computational medicine and biology (CMB) will inspire the development of the next generation of human body trauma injury models, involving several pathophysiology submodels including hemodynamics, respiration, perfusion, metabolism, hypoxia/ischemia, immune responses, neurochemistry, pharmacology, and others. This process will be conducted in parallel with precise, well-instrumented experimental tests on animal models.

The reduced models either are derived from fundamental laws of physics (algebraic expressions or simple ordinary differential equations, ODEs), with parameters obtained from model calibration on experimental data or from "curve fitting" of experimental data. High fidelity models are built based on similar laws of physics but are described with partial differential equations (PDEs) and use complex computational meshes generated from medical images. Between these two there can be various levels of approximations and sophistication. All models need calibration and validation before they can be used in the predictive form. Reduced models require few input parameters, are simpler to calibrate, and run very fast, but predict only gross parameters and their range of applicability is limited. High fidelity models require much more input for model setup (material properties, computational meshes, boundary conditions) and for validation (detailed field data as well as global/integral data). Their calibration is much more involved, requiring large computational resources, but their range of applicability is much wider and they provide a tremendous amount of spatio-temporal information. However, the development of high-fidelity models requires expertise in several disciplines and involves enormous resources. Development of mathematical models is an iterative process involving several cycles of computational and experimental tests. Figure 7-3 schematically illustrates the major components of the model development tasks.

High fidelity modeling of human body injury typically is organized in a "computational pipeline" (see Figure 7-3), involving several steps such as geometrical modeling of the body and experimental domain, image based mesh generation, model setup (material properties, boundary con-

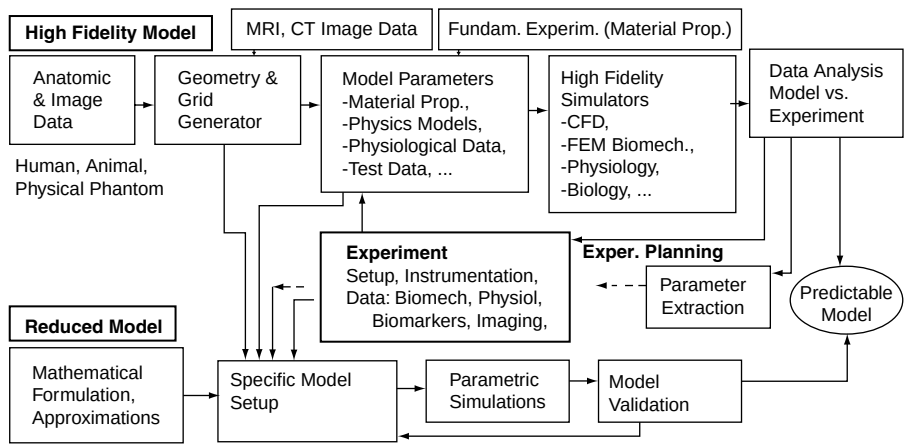

FIGURE 7-3
Schematic of a model development process involving iterative computational and experimental tests, model calibration, validation, and generation of model parameters for both high-fidelity and reduced models.

ditions, submodels), coupled multiphysics simulations, graphical post processing of massive simulation results, and model calibration/validation tasks. Note that high fidelity modeling results can be used to extract parameters for reduced models (broken arrows in Figure 7-3) and as an input for experiment planning. Computational modeling of blast injury and resulting trauma is extremely challenging as it involves several disciplines (gas dynamics, structures dynamics, biomechanics, physiology, pathology, biology, biochemistry), large range of time scales (microseconds of blast wave propagation to days/weeks of pathophysiology injury events), and dimension scales (micron scale alveoli or vascular capillary to meters scale human size and distance from explosion site). Comprehensive modeling of the blast wave lung injury should include several components:

- Energy release and shock wave formation in the explosive device
- Propagation of blast wave in air and reflections/diffractions on solid walls and objects
- Shock wave impact on and interaction with the human body
- Biodynamics of a flexible human body resulting from the shock wave loads
- Pressure wave interaction within the human body (e.g., thorax, head, abdomen, extremities)
- Wave absorption on protection devices (e.g., vests, aprons, etc.)
- Biomechanics of fluid-structures interaction of the pressure wave with the lung parenchyma, brain tissue, or other organs
- Pathophysiology of the lung/brain tissue including hemorrhage, edema, embolism
- Biological and biochemical responses of cellular injury and biochemical signaling metabolic, inflammatory, immune, apoptosis, repair, and other pathways
- Systemic responses including vasospasm, hypoxia, ischemia, trauma, and shock
- Resuscitation procedures and potential pharmacological treatment, and recovery

An integrated comprehensive multiscale modeling framework for high fidelity simulation of injury of the human body exposed to explosion blast wave involves several spatial resolution scales:

- **Virtual incidence scene**. CFD models of blast propagation in air and shock wave reflection from objects (e.g., walls, ground, etc.)
- **Body dynamics model**. Fluid-Structure Interaction (FSI) model of shock wave loading on a human body, flexible human body biodynamics (translocation) in space, and impact on walls/ground
- **Pressure wave propagation in human body**. Biomechanics of pressure wave propagation in the human body organs, wave reflections, and absorption (viscous dissipation)
- **Organ tissue biomechanics and pathophysiology of injury**. Detailed analysis of tissue stress/stains, deformations, changes in tissue perfusion, potential tearing of tissues (e.g., alveolar septa in the lung) or vascular structure, which may lead to hemorrhage, edema, emboli, hypoxia, ischemia
- **Cellular responses**. Secondary injury from biological and metabolic responses to ischemia, hypoxia, immune and inflammation responses, which may lead to cell apoptosis
- **Systemic responses to injury**. Changes in systemic hemodynamics including autoregulation, respiration, metabolism, activation of immune responses, trauma, and shock

Figure 7-4 presents a schematic of multiple models, the data transfers between various scales, and example simulation results obtained with CFDRC models (Przekwas et al. 2004; Ding et al. 2005; Imielinska et al. 2006). The biggest scale "virtual scene" CFD model of blast shock wave propagation in an urban setting provides detailed pressure and wind loadings on human bodies affected by the shock wave. Those data are used for modeling human body dynamics (translocation in air) and for pressure wave penetration in the human body, and stress/deformation biomechanics of various tissues and organs (thoracic cross section and respirating lung shown in Figure 7-4). A biomechanics-based lung tissue injury model is used to estimate the degree of alveolar injury (septal breakup, hemorrhage, and edema) in a fluid and gas (CO_2, O_2) exchange lung model. Ultimately the whole body systemic model of cardiopulmonary respiration/circulation and metabolism, with the "injured" lung model will be able to simulate secondary injury events including hypoxia, ischemia, immune responses, and medical treatment.

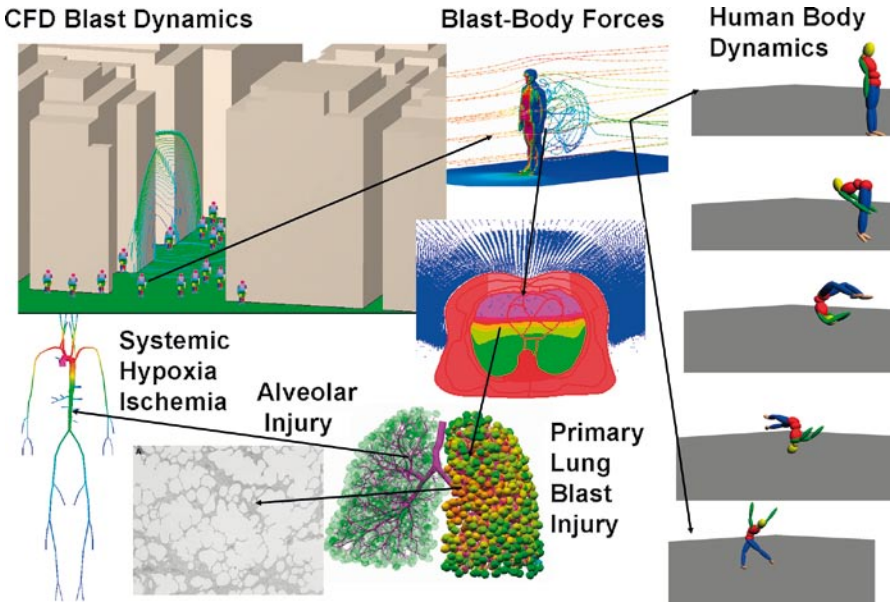

FIGURE 7-4
Schematic of a multiscale simulation environment for modeling blast injury events and example computational results (arrows indicate data transfer flow for subsequent models).

It is apparent that the mathematical modeling of blast wave human body injury with high fidelity models requires a good understanding of human body anatomy, physiology, and injury mechanisms. The next section presents a brief overview of these from the modeling point of view.

Human Body Anatomy—Blast Injury Modeling Perspective

When a blast wave impacts the human body, the entire body will be exposed to the pressure wave. When the body is in close proximity to an explosion, all organs including the brain, lung, and even the extremities will be vulnerable to injury, typically with fatal consequences. At larger distances, primarily the brain and air-filled organs (lung, ear, intestine) are prone to primary blast injury. Advanced computational modeling of human body blast injury requires anthropometric and anatomical data to generate the human body geometry and computational mesh. Human body dynamics models, such as the Articulated Total Body (ATB) or MADYMO models (Cheng & Rizer 1998; Przekwas et al. 2004; Haeppee et al. 2003) illustrated in Figures 7-5A and 7-5B, represent the body by a small number of body segments and joints, which need only approximate dimensions and masses of main organs (thorax, head, led, arm, etc.). The input data to these models can be obtained from complete

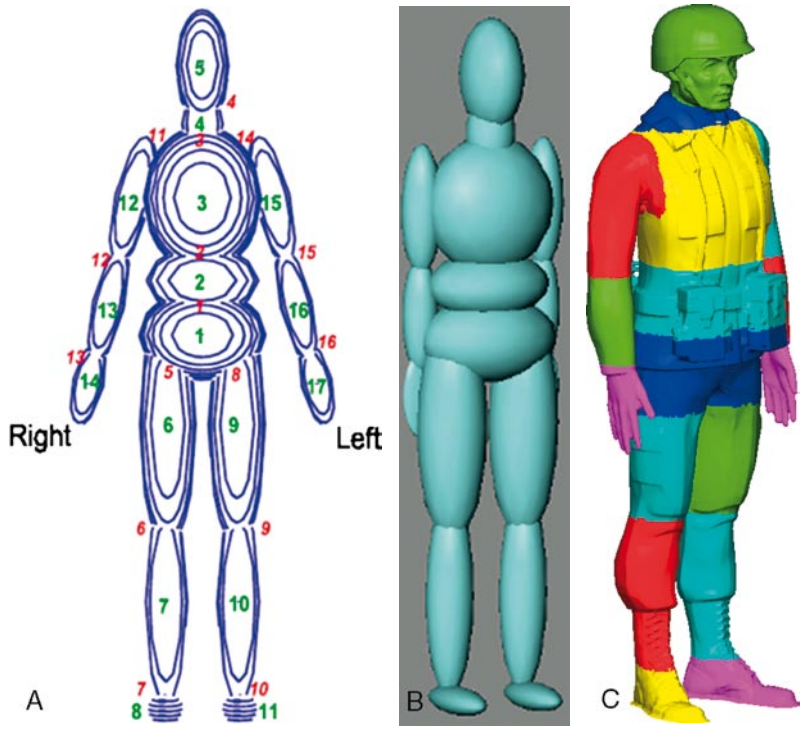

FIGURE 7-5
Various geometrical representations of a human body for bio-dynamic simulations.

Continued

human body surface scans and basic anthropometry, as shown in Figure 7-5C. Note that the body surface (and volume) has been divided into segments corresponding to the ATB body segments for two reasons: (1) to calculate the subject specific body segment masses and positions, and (2) to calculate the blast wave pressure and wind forces and moments on individual body segments. Cheng et al. (1994) developed the GEnerator of BOdy Data (GEBOD) program that can be used for automated generation of rigid body models for ATB simulations using ellipsoid body segments with individual geometry and mass properties. High resolution body scans can be obtained with existing commercial laser scanners and large databases of human subjects are available. One such database is the CAESAR databank created by scanning thousands of individuals in the United States and Europe, with an example human body scan shown in Figure 7-5D (Robinette & Daanen 2006). The surface body scan data is typically available in the form of triangulated surfaces in the STL format (stereolithography data format in an ASCII or binary file used in manufacturing). Computation of blast wave pressure/wind

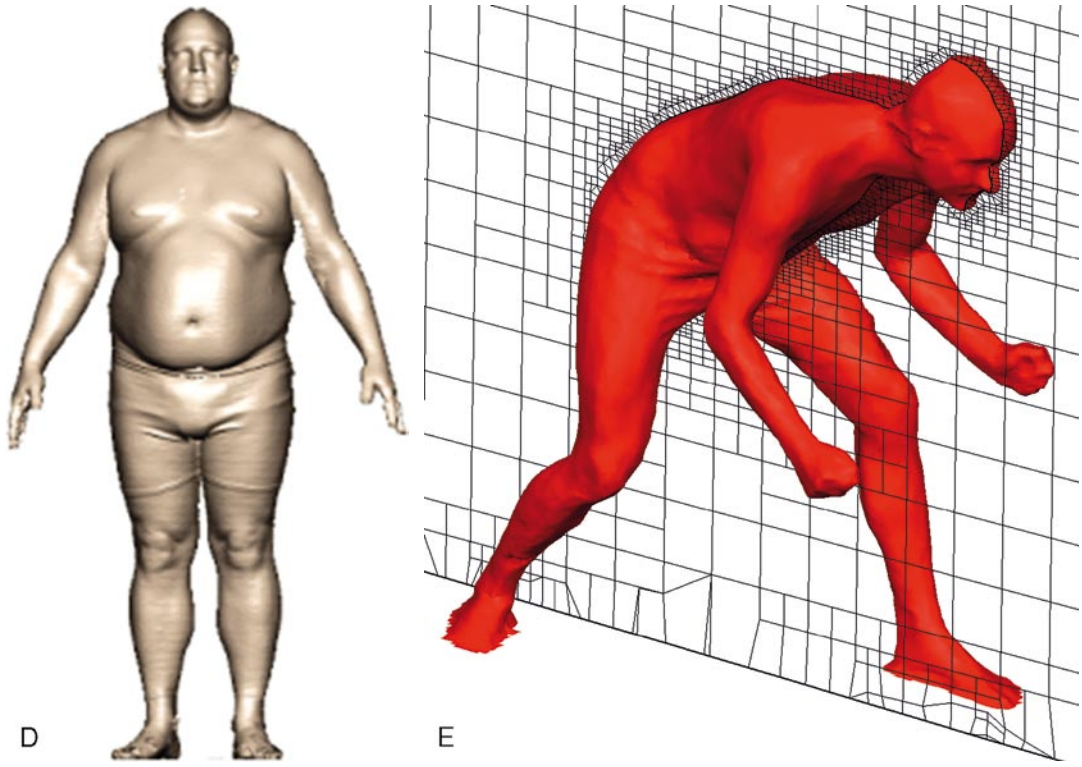

FIGURE 7-5
Cont'd

loads on the human body is typically performed using CFD software on 3D grids as shown in Figure 7-5E. As discussed later, generation of 3D body-conforming grids that allow modeling of body translocation in air is very challenging. Computation of human body dynamics also requires physiological input in the form of body joint parameters/constraints and potentially muscle tension data. Results of such a model provide spatial position of the body/organs and forces on the body segments during impact of the body on the ground or other rigid objects.

Computational modeling of the primary (blast) or secondary (ballistic fragment) injury of internal body organs requires human body internal organ data, including geometrical, morphological, biomechanical, and physiological data. For example, multidimensional modeling of pressure wave propagation in the human lung is performed on the computational mesh of the entire thoracic body including all tissues, and depending on the situation, protective body armor. Detailed information about human body internal geometry can be obtained from segmented medical imaging

data such as MRI or CT, which are available in the form of 2D "voxel" data (e.g., 512 × 512 volumetric pixels, or voxels, with annotated tissue type) for several cross sections along the body. The National Library of Medicine of the National Institute of Health (NIH) has established a "Visible Human" open access database with high resolution, anatomically detailed, three-dimensional representations of human male and female bodies (Spitzer et al. 1996; Spitzer & Scherzinger 2006; http://www.nlm.nih.gov/research/visible/visible_human.html). The data was obtained by making color photographs of sectioned "fresh frozen" cadaver specimens. It consists of 1,871 transverse cross sections of a male and 5,000 slices for a female, with voxel resolution of 0.32 × 0.32 mm. Artifacts resulting from freezing, container support, and internal postmortem distortions can be identified, such as collapsed lung or a "flat butt" (Ackerman, 2002). Despite these limitations, such high resolution data can be used to generate detailed 3D geometry and computational meshes for human body biomechanical or physiological simulations. A similar set of data has been established for a Chinese male and female (Zhang 2004; http://www.chinesevisiblehuman.com/). The Visible Human data has been used by scientists worldwide for all types of biomedical mathematical modeling.

Computational modeling of blast lung injury is conducted using detailed geometry and morphology of the thoracic cavity, including skeletal, muscular, and thoracic and abdominal organs. The thoracic skeletal structure is made up of 12 pairs of ribs, 12 thoracic vertebrae and intervertebral discs, a sternum, and costal cartilage. It provides support and protection to internal organs including the heart, lungs, pleurae, trachea, and great vessels. Figure 7-6 shows an annotated diagram of the thoracic cage. To generate a finite element mesh of the thoracic cavity, a clear definition of the skeletal and tissue geometries has to be developed. Manual generation of a thorax computational mesh is very tedious and not practical. Automated generators of triangulated surfaces of the skeletal system and all organs are not available, yet are urgently needed. After triangulated surfaces of bones, internal organs, and the skin are established, a 3D tetrahedral mesh of the entire body can be generated with available and well-established unstructured grid generators. In biomechanics, bones are modeled as linear elastic rate-dependent materials and muscles and soft organs as hyperplastic or viscoelastic materials (Fung 1993; Roberts et al. 2006). Unfortunately, for viscoelastic materials the existing FEM software works much better on hexahedral meshes than tetrahedral. This prob-

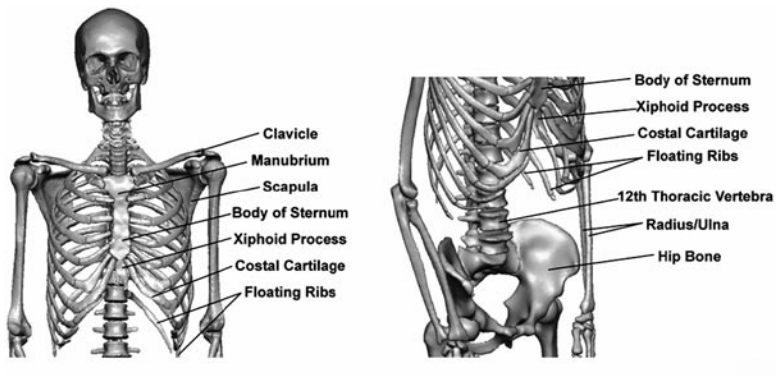

FIGURE 7-6
Surface anatomical skeletal solid structures—a starting point for FEM mesh generation for computational biomechanics simulations.

lem can be resolved either by developing automated hexahedral meshers, robust viscoelastic tetrahedral elements, or preferably both. Geometrical representation, meshing, and FEM modeling of the lung and other internal organs is discussed later.

Three-dimensional computational modeling of the thoracic cavity and lung biomechanics and ballistic or blast injury requires a large computational mesh that can resolve transient propagating pressure waves in the body. For 3D human body FEM biomechanics of blast wave propagation problems a mesh of at least 10^6 elements, preferably with solution adaptive mesh refinement and nonlinear material properties, would be needed. Such large scale problems can be solved only using explicit FEM solvers, which suffer from strict time step size limitations, rendering the problem computationally very expensive even with parallel computers. The state-of-the-art FEM human body biomechanics models (Roberts et al. 2006) use approximately 250,000 elements to solve mechanical lung injury. An intermediate step before full 3D models are established is to employ 2D models of the thoracic cavity.

Geometric modeling and meshing of inhomogeneous internal organs such as the blood-filled heart and major vessels, or air-filled lungs, or part of the gastrointestinal track is even more challenging. Lungs are particularly cumbersome for FEM models because of the large amount of air content that cannot be represented by typical FEM materials (elastic or viscoelastic). Until now it has not been resolved if macroscopic lung parenchyma should be represented as a porous fluid or viscoelastic solid. Challenges and modeling methods for macroscopic and microscopic models of lung parenchyma are discussed in the next section. Three-dimensional models of lung bio-

mechanics face another major numerical challenge—"contact with friction" between visceral and parietal pleurae. The visceral pleura is attached to the lung and the parietal pleura lines the internal surface of the thoracic wall and diaphragm, and completely encases the visceral pleura and lungs. The space between the two pleura is filled with pleural fluid, which acts as a lubricant during pleural sliding on each other during respiration. If meshed organs contact and slide on each other they create a tough numerical problem of modeling interface forces and mesh interaction (nonpenetration). The problem can be solved correctly but the numerical algorithms are computationally very expensive.

Recently CFDRC has used the Visible Human data to generate geometry and computational meshes for modeling blast wave penetration through a human thorax. Figure 7-7A presents an example slice across the Visible Human male thorax with segmented major organs including lungs, ribs, left/right atrium, left/right ventricle, and others. The geometry and tissue marker data was used to generate a computational mesh. Coupled blast wave impact and FEM pressure wave biomechanics simulations were performed on a 2D computational mesh, shown in Figure 7-7B, covering not only the body tissues but also the surrounding air through which the blast wave impacts the body. To simplify the simulations for the frontal (anterior) blast wave impact, both arms were removed during the mesh generation. The computational mesh conforms to the boundaries of individual organs, for which organ specific material properties were specified and specific inter-organ boundary conditions were defined to discriminate between dissimilar materials such as rigid organ attachment (muscle to bone) or sliding interface (lung on thoracic wall).

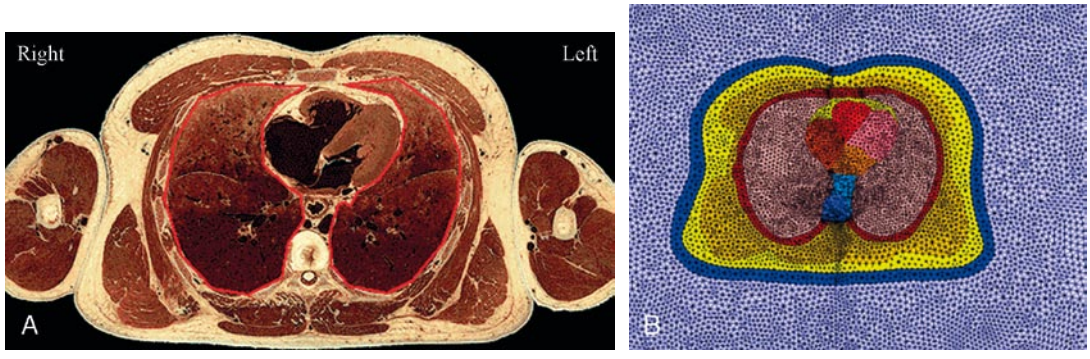

FIGURE 7-7
Visible human data for a transverse section through ***(A)*** *the thorax and an example unstructured computational mesh covering both the human body as well as* ***(B)*** *the surrounding air used for modeling blast wave penetration through the thorax and lungs and tissue biomechanics.*

The FEM biomechanics stress/deformation model uses several organ-specific material properties such as density, sound speed, Young modulus, porosity, and others. The mechanical properties of human tissues and bones depend on several factors including age, sex, shape, and size, but also on the loading direction. Extensive research has been conducted to obtain biomechanical tissue properties (Fung 1993; Yoganandan & Pintar 1998). Typically the sternum and the ribs are modeled using linear elastic rate-dependent models. Unlike bone, material properties of tissues and internal organs, and the lung in particular, are more difficult to model. Material properties of the lung are discussed in the next section. Material properties of the heart and aorta exhibit strong anisotropy and typically are represented as either hyperelastic or viscoelastic (Yen 1999; Deng, Kong & Ho 1999).

Biomechanical simulation of blast pressure wave propagation in the thoracic tissue can provide valuable information of potential injury. For example, the results of thoracic tissue biomechanics can be used to identify regions of largest strains, deformations, and stresses within the lung, heart, major vessels, and other tissues. These parameters in turn can be used for modeling organ pathophysiology resulting from the biomechanical injury.

Image- and Anatomy-based High Fidelity Model of a Lung

The lung is the most susceptible organ to mechanical injury resulting from blast pressure waves. A high-fidelity model of lung physiology and blast wave injury can be developed based on medical imaging data and anatomical and physiological information. As mentioned earlier, the Visible Human data can provide excellent anatomical resolution of solid tissues such as bones and muscles, but is inadequate for air-, blood-, or liquid-filled tissues such as lung, vasculature, or brain cerebrospinal fluid spaces. Fortunately the latest developments in high-resolution X-ray computed tomography (CT) imaging provide good quality of geometrical and morphological data. For example, the latest multislice spiral CT scanners can generate over 300 image slices of the chest with slice thicknesses of less than 1 mm, and lung atlas-based segmentation can provide excellent 3D resolution of the lung (Tschirren et al. 2005; Zhang, Hoffman & Reinhardt 2006). Such data has been used to generate a novel high fidelity physiological model of a lung applicable for blast injury analysis (Ding et al. 2005). Figure 7-8 presents example X-ray CT images for lung lobes and for an upper respiratory tracheobronchial air trunk (Ding et al. 2005) used by CFDRC to generate a high fidelity model of a lung.

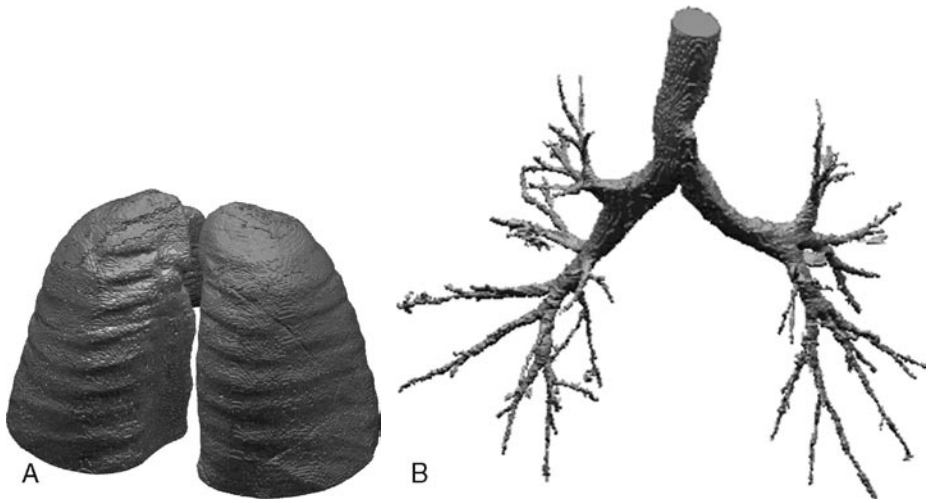

FIGURE 7-8
Lung lobes and tracheobronchial airway geometry from medical X-ray computed tomography imaging (Ding et al. 2005).

Most of the previously reported lung physiology models simulate only a small part of the bronchial tree whereas whole-lung models typically are represented by multicompartmental models (Athanasiades et al. 2000). The whole-lung lung model developed by Ding et al. (2005) includes not only the complete air track from the trachea to the alveolar sacks, but also pulmonary circulation, gas exchange, and a direct interface to a whole body circulation–respiration–metabolism model. This section presents the details of the model geometry, and the next section presents example simulation results.

The primary role of the lungs is to facilitate gas exchange between pulmonary airways and the pulmonary blood circulation. The airways are organized into a branching network of air-filled tubes starting from the trachea (1–2 cm in diameter), which divides into the left and right bronchi (see Figure 7-9B), entering into the right and left lobes. At the third generation of the airway tree, the airways, called bronchioles, range in diameter from 1 mm to 5 mm. The bronchial tree further divides into a bronchial tree up to the seventeenth generation of terminal bronchioles. Beyond these, the airways continue to branch and lead to the alveolar ducts, and ultimately terminate in the huge number of thin-walled alveolar sacs, the site of air–blood gas exchange. The sponge-like lung parenchyma is composed of roughly polyhedral shaped alveoli. In humans the parenchyma constitutes 90% of the total volume of the lung. Alveolar walls are built of fibrillated connective, muscular, and elastic fibers, and support a network of pulmonary capillaries. The typical mean number of alveoli in a human lung is approximately 480 million and the mean size of a single alveolus

is approximately 100 to 400 μm, with the largest on the surface of the lung, at the borders and at the apex, and the smallest in the lung interior (Ochs et al. 2004). The number of alveoli is proportional to the lung volume. The alveoli are surrounded by a network of capillaries approximately 5 μm in diameter, embedded in a very thin alveolar-capillary membrane (0.2–0.6 μm), which is traversed by oxygen and carbon dioxide during the gas exchange process.

Since lung function varies regionally and because the blunt injury is usually not uniformly distributed in the lungs, it is essential to study the lungs respiration physiology and injury using a 3D geometry defined by the tracheobronchial tree, individual lobes, and the approximate representation of the complete bronchial/alveolar tree. A high fidelity lung physiology and injury model should solve for airflow, pressure, mechanical tension, and gas exchange within the 3D geometry of the lung parenchyma. The first task of lung simulation is to generate the airway geometry and computational mesh from medical images (see Figure 7-8). Even the best resolution lung image provides only four to five branching levels of the tracheobronchial tree. The remaining child branches have to be generated using suitable mathematical algorithms (Karch et al. 1999, 2003; Kitaoka, Ryuji & Suki 1999; Tgavalekos et al. 2003). The starting point of our lung geometrical model was the mesh, shown in Figure 7-9A, generated from the root tree image of Figure 7-8B. Higher generation branches were populated using a tree generation utility based on an optimization-based mathematical algorithm (Karch et al. 1999, 2003). The tree generation utility developed by CFDRC reads an initial air tree and the shape of the lung lobes (in voxel format) shown in Figure 7-8, and creates the cascade of child branches inside the lung volume with a user-specified total number of termination branches. The branching tree is optimized to achieve uniform air supply of the lung volume, and uniform and minimum pressure drop. Figure 7-9B presents the generated geometrical model of the air tree in the lung lobes. In this model the tips of the tree are terminated with "effective alveoli" as shown in Figure 7-9C. The geometrical parameters of "equivalent alveoli" such as gas exchange surface area, volume, and air-blood diffusion distance are calculated based on the subject specific lung data, typical number and size of alveoli, and the morphology of alveolar wall structures (surfactant thickness) as described earlier.

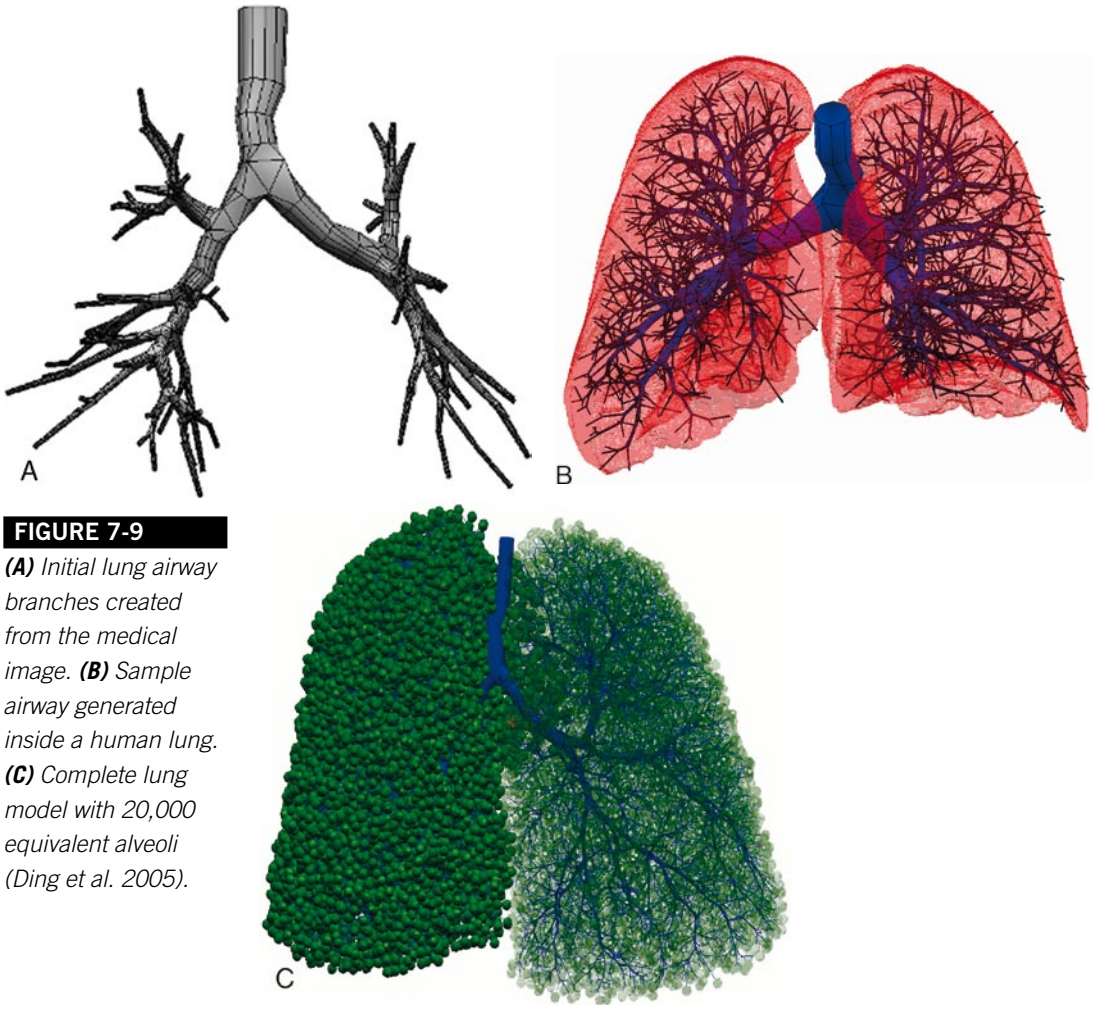

FIGURE 7-9
(A) *Initial lung airway branches created from the medical image.* ***(B)*** *Sample airway generated inside a human lung.* ***(C)*** *Complete lung model with 20,000 equivalent alveoli (Ding et al. 2005).*

In the complete high fidelity lung respiration physiology model the entire geometry is time-dependent, as the mesh of the entire tree and all alveoli deform in the 3D space (expand/contract) following the diaphragm motion during the respiration cycle. That periodic change in the lung volume geometry results in air being inhaled into the lung during lung expansion and expelled from the lung during contraction in each respiration cycle. Mathematical and physiological details of the lung model and example simulation results are presented in the next sections.

MODELING EXPLOSION BLAST—HUMAN BODY DYNAMICS AND BIOMECHANICS

Models of Explosion Blast Gas Dynamics

Mathematical modeling of explosions and shock waves has been conducted using either simplified analytical methods (Taylor 1950; Henrych 1979; Sedov 1993) or numerical methods for solving full gas dynamics equations on powerful computers (Woodward & Colella 1984; Harten et al. 1987; Baum, Luo & Lohner 1993; Kato et al. 2006). Blast wave properties and loads on structures can be calculated from analytical models only for idealized conditions (e.g., spherical blast) or for simple geometries (e.g., shock tube) using Sedov self-similar solutions (Sedov 1993). Sedov analytical solutions for nondimensional velocity, pressure, density, absolute temperature, sound speed, and shock location (Sedov 1993, Eqs. 11.15 and 11.16) are expressed in terms of an independent variable and a similarity coordinate (nondimensional distance) parameter V, which is expressed by $V = vt/r$ (where v is the velocity, t the time, and r the radial location). These solutions are normalized by the state variables behind the shock (Sedov 1993, Eqs. 11.2, 11.3, 11.4) calculated as a function of time, t, and two input parameters: E (energy release in blast) and ρ_1 (density of the undisturbed gas). Direct physical gas properties along the radial distance at any time instant can be calculated by multiplying the nondimensional solutions by the corresponding state variables. These solutions could be used as a first approximation to compute time-dependent blast wave loads on structures (e.g., human body) positioned at a distance from the explosion site.

For more complex problems, Computational Fluid Dynamics (CFD) methods have to be used. Computational modeling of blast waves is very challenging because, to capture the details of a propagating shock wave with steep property gradients in the shock wave front, the problem has to be solved as time dependent on a very fine (10^6–10^8 grid nodes) mesh. In a typical scenario, a micrometers thin shock wave propagates in meters size domain with supersonic speeds of 1000 m/sec with the primary shock expansion duration lasting tens to hundreds of ms. To minimize the resource requirements (mesh size, time step, computing time), over the years many sophisticated high-accuracy numerical schemes have been developed such as FCT (Baum et al. 1993), approximate Riemann solvers, TVD, ENO (Harten et al. 1987), PPM (Woodward & Colella 1984), and others. Because the fine mesh is needed only in the shock wave, zone adap-

tive mesh refinement grids can be used (Coirier & Bayyuk 2002) and CPU times can be reduced by using parallel computing.

Computational modeling of shock wave physics in an open/closed environment involves solution of Navier-Stokes (N-S) equations:

$$\text{Continuity:} \quad \frac{\partial \rho}{\partial t} + \nabla \cdot (\rho v) = 0 \tag{7.10}$$

$$\text{Momentum:} \quad \frac{\partial}{\partial t}(\rho v) + \nabla \cdot (\rho v v) = -\nabla p + \nabla \cdot \tau + \rho F \tag{7.11}$$

$$\text{Energy :} \quad \frac{\partial}{\partial t}(\rho E) + \nabla \cdot (\rho v E) = \nabla (k \nabla T) - \nabla (p v) + \nabla (v \cdot \tau) + \rho S_E \tag{7.12}$$

$$E = e + \tfrac{1}{2}\left(u^2 + v^2 + w^2\right) = e + \tfrac{1}{2}U^2$$

where v is the velocity vector, p is the pressure, ρ is the fluid density, τ is the viscous stress tensor, F is the body force (e.g., gravity), E is the total energy, e is the enthalpy, T is the absolute temperature, and k is the heat transfer coefficient. The stress is computed as:

$$\tau = \mu \cdot [\nabla v + (\nabla v)^T] - \tfrac{2}{3}\mu_{etf}(\nabla \cdot v)\delta \tag{7.13}$$

where μ is the viscosity of the fluid and δ is the unit tensor. In several high speed gas dynamics problems the viscous stress term is negligible and the N-S equations reduce to Euler equations. For most shock dynamics problems in air, Euler equations are sufficient. Analysis of sound and blast waves in various elastic media including air and the human body require a clear definition of the speed of sound. In general the speed of sound, c, is defined as:

$$c = \sqrt{K / \rho} \tag{7.14}$$

where K is the stiffness coefficient or bulk modulus defined as a ratio of stress (force F per unit area **A**, or pressure p) to the relative volume change:

$$K = \frac{F/A}{\Delta V / V} = -V\left(\frac{dp}{dV}\right) = \rho\left(\frac{\partial p}{\partial \rho}\right) \tag{7.15}$$

In an ideal gas (e.g., air), $K = \gamma^* p$, where γ is the property known as the isentropic expansion factor (or ratio of specific heats, in air $\gamma = 1.4$) so the sound speed can be calculated as

$$c_{air} = \sqrt{\gamma \cdot p / \rho} \tag{7.16}$$

For reference, the speed of sound in air is 344 m/sec (770 mph); in saltwater, about 1500 m/sec; and in freshwater, 1435 m/sec. Sound speed in solids and biological tissues such as the lung is discussed next.

The computational simulation of traveling shock waves and wave diffraction on objects requires high resolution in both space and time, which in turn requires a high mesh density and high numerical accuracy, especially in the shock wave interaction regions. Shock shape and position in time-space can only be found as part of the solution. It would be prohibitively expensive to use a fine mesh everywhere in the domain. An alternative technique is to use a locally refined solution-adaptive mesh with a finer mesh near the shock. CFDRC has developed the HAMR (Hierarchical Adaptive Mesh Refinement) CFD flow solver for simulation of blast wave explosions in urban areas (Coirier & Bayyuk 2002). The code uses solution (shock wave position) dependent adaptive Cartesian-Octree (in 3D) and Cartesian-Quadtree (in 2D) grids to simulate complex blast wave patterns in open space and in complex urban environments. The code was validated on several blast wave problems and was applied to simulate complex blast wave loads on buildings and on human bodies in open spaces, urban settings, and in closed rooms. Figure 7-10 presents two validation examples for a planar shock wave propagating in a quiescent gas (air 298°K) and impinging on an inclined wall. In both cases an adaptive Quad-tree mesh is used with the mesh adapted (refined) for regions with strong density gradients (shock wave). The first test case is the "regular" Mach reflection, a planar incident shock impinging on an inclined wall. The incident shock speed is M = 1.17 with a wall angle of 50°. When the shock arrives at the inclined wall corner it generates the "reflected" shock (or bow shock, as it looks like a bow) that propagates backward. In this case the primary shock is in contact with the inclined wall. The second case, a "single Mach reflection," is similar except that the wall angle is 25°. This time the reflected shock is more curved, with a short Mach shock created normal to the wall, and a triple point formed at a distance from the wall where the incident shock and Mach shock meet. These test cases have been experimentally investigated by Ben-Dor (1991) and Itoh (1991). Figure 7-10 presents predicted density contours and corresponding experimental interferogram images for both test cases, showing very good agreement.

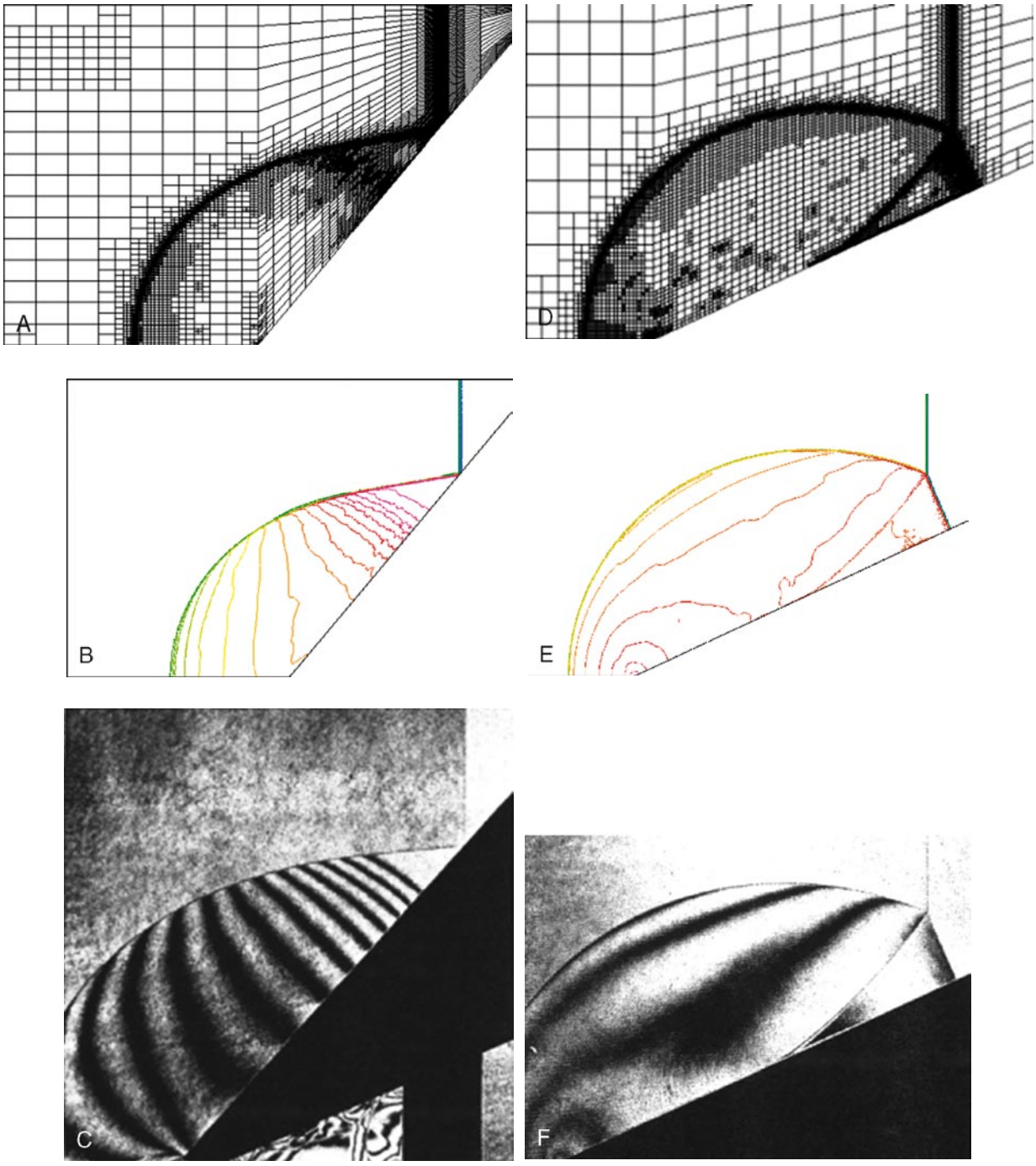

FIGURE 7-10 *Adapted grid, predicted density contours, and interferogram images (from Ben-Dor 1991) for a planar shock wave reflection, M=1.17 ramp angle* $\theta_{wedge}=50^{o}$ *and Ms=1.17 ,* $\theta_{wedge}=25^{o}$ *and Ms=1.17; the shock moves from left to right.*

CFD software tools can be used to simulate blast explosions in complex environments such as in urban areas (Coirier & Bayyuk 2002), buildings (Baum, Luo & Lohner 1995), aircraft (Baum, Luo & Lohner 1993), and other settings. Figure 7-11 presents an example explosion blast wave propagation and multiple reflections in an urban area (Coirier & Boyyuk 2002). Utilizing both a top-down and perspective view of the street, three time instance pressure plots of the unsteady shock wave development and the reflections/diffractions on the building walls are shown. It is feasible to include vehicles and individual people in the simulation scene and compute dynamic blast wave loads on objects and people and their dynamic translocation in air and their impact on walls and the ground. Those results could be used to compute human body injury. Both of these are discussed next.

Human Body Blast Waves and Wind Loads

Full understanding of blast wave interaction with the human body is possible if the human body is immersed in the computational domain of blast gas dynamics. At each time step during CFD simulations the loading on the body should be used to calculate the body deformation and

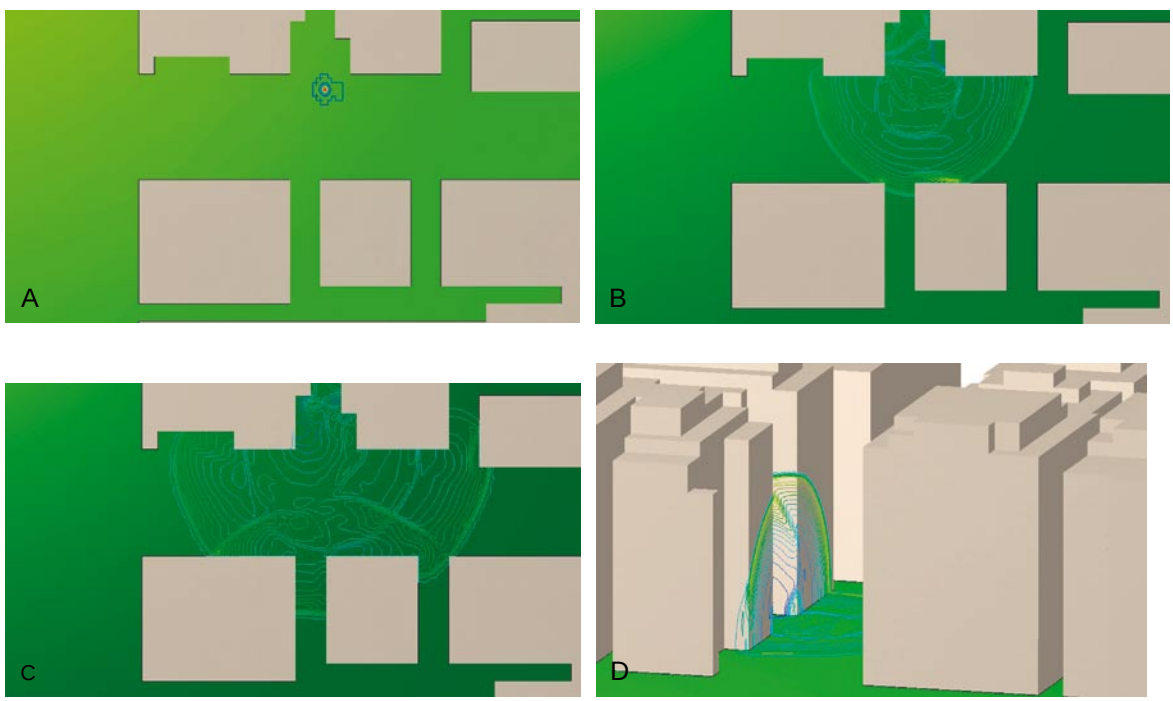

FIGURE 7-11
Time evolution of pressure loads resulting from a blast explosion in an urban area (Coirier & Bayyuk 2002).

translocation in air. To this author's knowledge such fully coupled blast wave–flexible human body interaction simulations have not been reported yet. It is a challenging task because of complex grid generation issues, the fluid-structures interaction problem, and human flexible body biomechanics. As a first approximation the body could be assumed to be rigid and the blast wave and wind loads could be recorded as a function of time and position on the body. That information could be used by available human body dynamics models (Cheng & Rizer 1998; Haeppee et al. 2003; Przekwas et al. 2004, 2005) to calculate body dynamics in a postprocessing mode. The same loads could be also used to compute pressure wave penetration of the human body tissue and resultant tissue/organs stress/deformation biomechanics. Figure 7-12 graphically explains the major steps in modeling human body exposure to a gust of wind in an experimental facility (at AFRL/HEPA, Wright Patterson, OH) and collection of human body biomechanical parameters such as body loading, forces and moments on various organs, body segments, and joints. A subject-specific human body scan has been meshed and immersed in an entire test facility using an

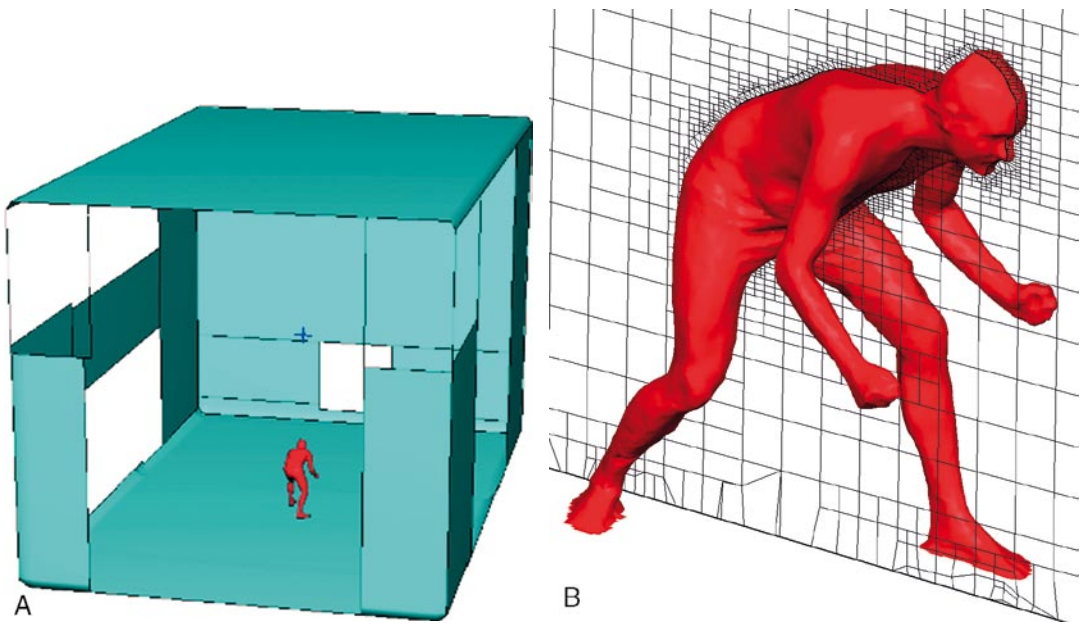

FIGURE 7-12 *Computational modeling of high speed wind interaction with a human body, pressure loads on the body, and calculation of forces and moments on various body parts for body biomechanics using ATB model (Wilkerson & Przekwas 2005).*

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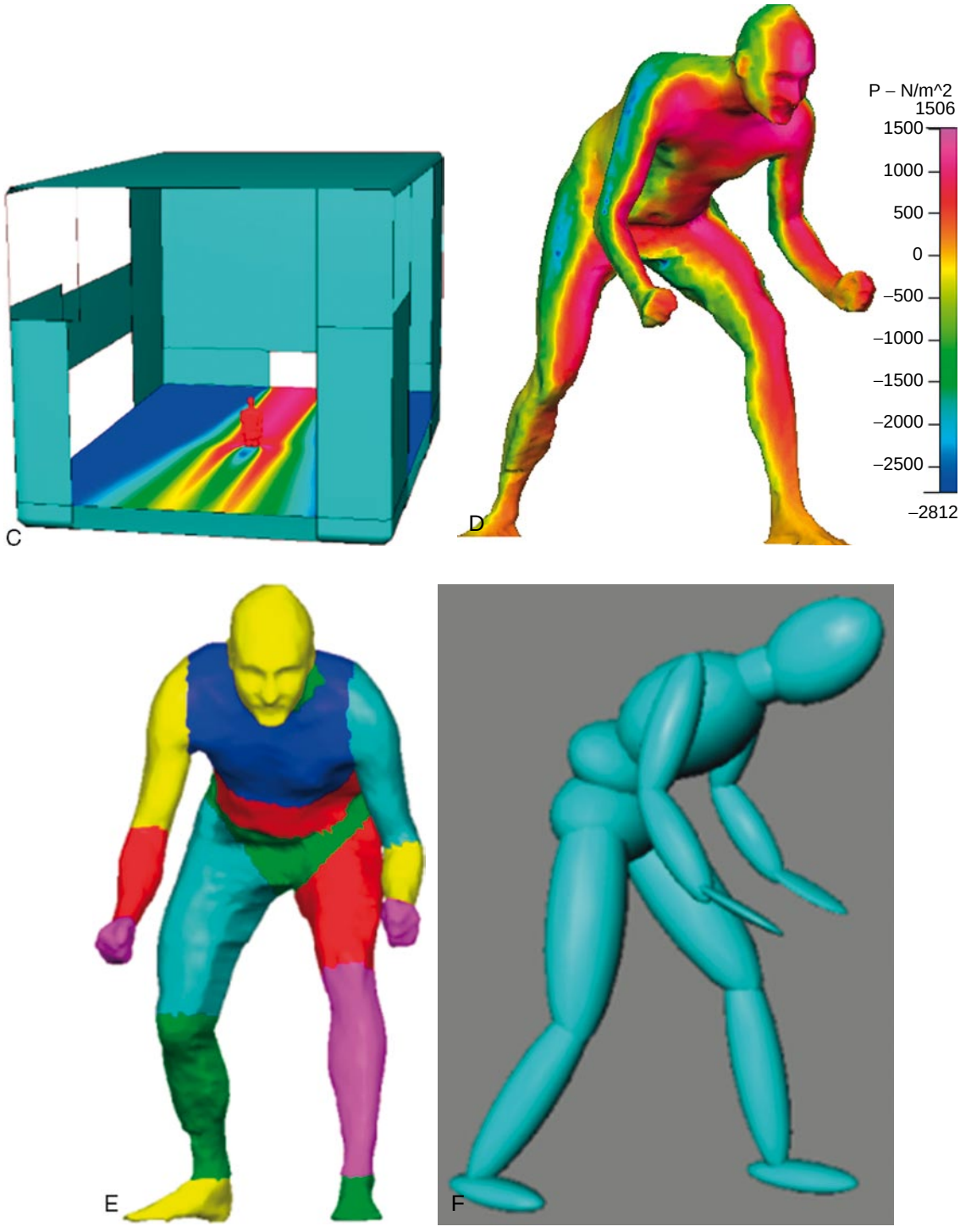

FIGURE 7-12 *Cont'd*

adaptive Cartesian mesh (Wilkerson & Przekwas 2005). CFD computations were performed assuming a rigid body in the flow field (in several different body postures and positions) and the pressure and wind shear loads calculated on the entire body surface (Figure 7-12). The body was divided into numerous segments corresponding to the body segments (Figure 7-12F) used by the Articulated Total Body (ATB) software (Cheng & Rizer 1998; Przekwas et al. 2005). Biodynamic modeling of the flexible body was performed to calculate the forces and moments on body joints and to assess the overall stability of the body. Modeling of body dynamics during kinetic or blast wave impact could be also performed using ATB.

If the wind blast is constant the above test case can be simulated as a steady state problem and no mesh adaptation is needed except initial adaptation to the human body shape, which significantly simplifies the modeling task. But a blast wave–human body interaction is transient and, depending on the numerical scheme used, millions of time steps have to be computed, large numbers of mesh adaptations performed, and huge amounts of 3D data fields accumulated. Przekwas et al. (2004) performed several computational simulations of a blast wave interaction with a surrogate human body in closed spaces to analyze the influence of body position relative to the explosion site, explosive power, distance to the wall, and other parameters on the human body blast loads. Figure 7-13 presents example simulation results for an explosion blast in a room occupied by a soldier. It is assumed that a rigid soldier body is standing in a rigid-walled room with dimensions (length 5 m, width 5 m, height 2.7 m). In this case the soldier (height 1.80 m) is standing in the vertically upright position with the axis of the soldier's body passing through the point $(x, y, z) = (1, 2.5, 0)$, as indicated in Figure 7-13.

The blast was created by a 0.5 kg TNT-Equivalent explosive charge, detonated at the location $(x, y, z) = (1.5, 1.5, 1.0)$. Figure 7-13A presents the initial instant of the explosion to the right side of the soldier and Figure 7-13B shows the shock wave front adapted mesh just before the wave hits the soldier. Figure 7-13C presents the pressure contours on the surface of the surrogate rigid soldier after $t = 0.002$s from the detonation instant, with the leading blast wave partially engulfing the soldier's body. The front of the blast wave is shown in translucent gray. The figure also shows that the blast wave has reached and reflected from the floor of the room, but has not yet reached the ceiling. In several simulations the surrogate

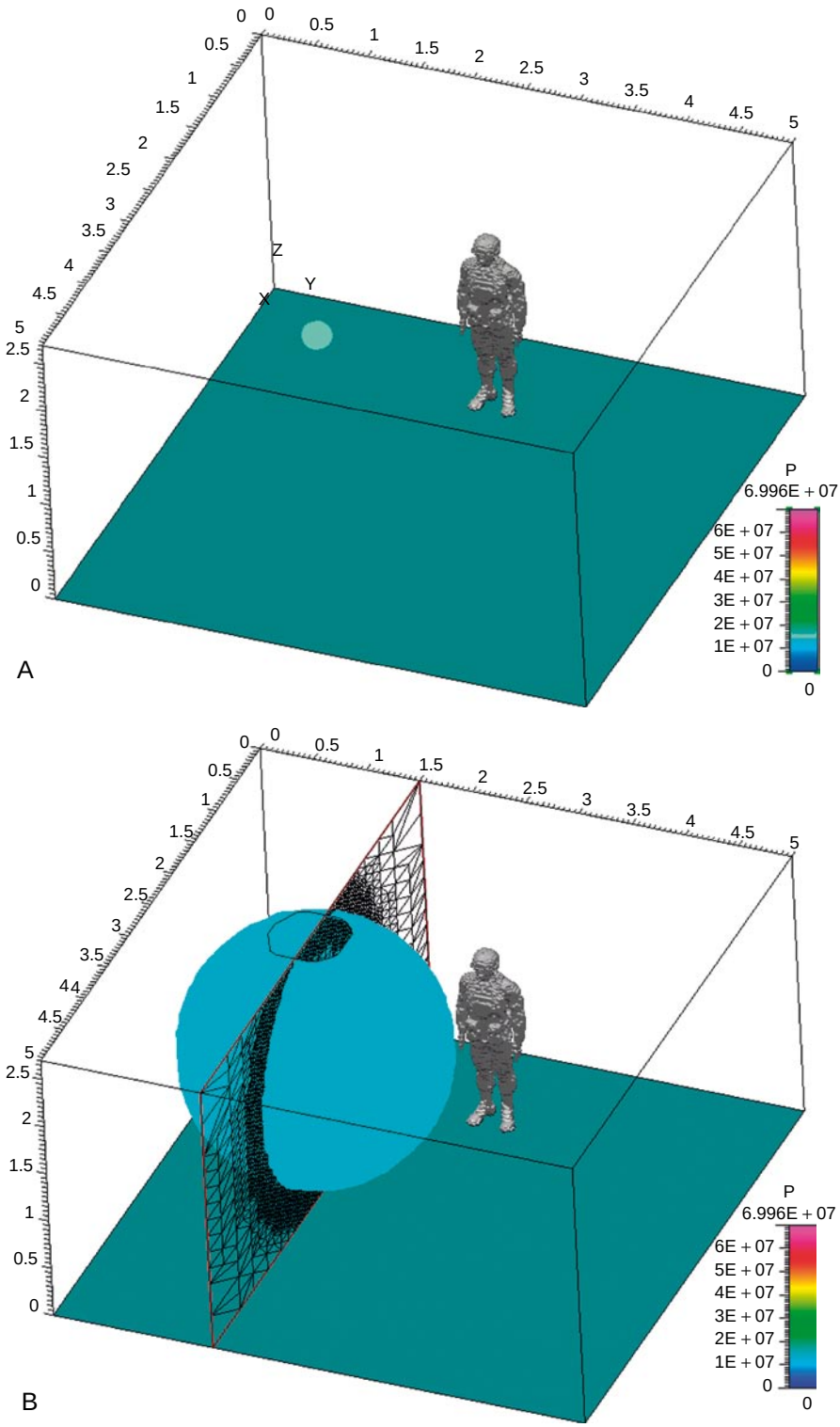

FIGURE 7-13
Simulation results for an explosion in a room occupied by a Soldier.
(Continued)

FIGURE 7-13
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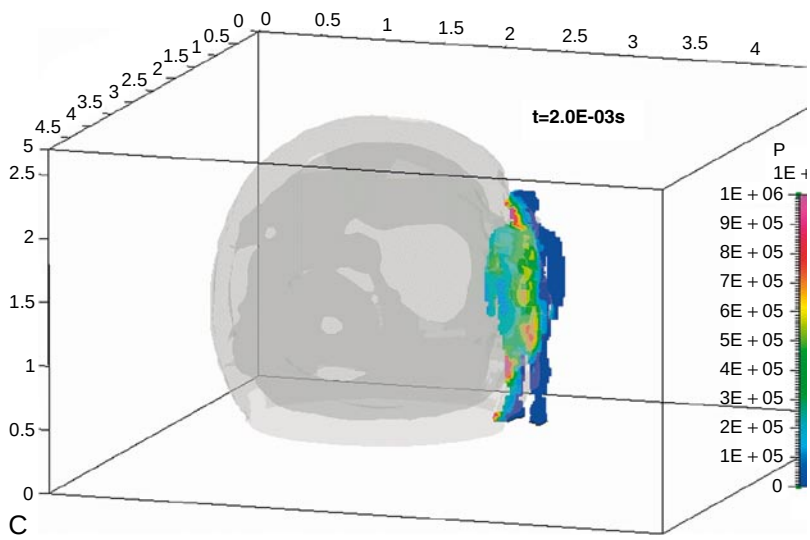


soldier's body was "instrumented" by placing pressure sensors on the body surface. The parameters that were varied between the individual simulations included:

- Initiation location of the blast wave
- Strength of the blast wave, in terms of a TNT-mass-equivalent explosive charge
- The location of the soldier in the room, in particular the distance of the soldier from the rear wall

The primary quantity of interest in these simulations was to record pressure sensor history readings at 10 locations on the front and back of the soldier's left chest. That information can be used to design personnel protective armor and to assess the potential injury criteria. Figure 7-14 shows the pressure history at the 10 monitoring points on the soldier's chest for the 0.25 m soldier-wall distance case with a weak (0.2 kg TNT) charge. The same room and soldier are used but the soldier's position is at $(x,y,z) = (0.25, 2.5, 0.0)$ and the blast is located at $(x,y,z) = (3.5, 3.5, 1.5)$ in the room. Note that the surrogate soldier's body was placed at a distance of 0.25 m from the rear wall while the explosive charge was in the middle part of the room. The figure shows that the peak pressure is recorded on the front chest as the primary blast wave collides with it, and shows the slight time delays between the pressure pulses sustained at the different

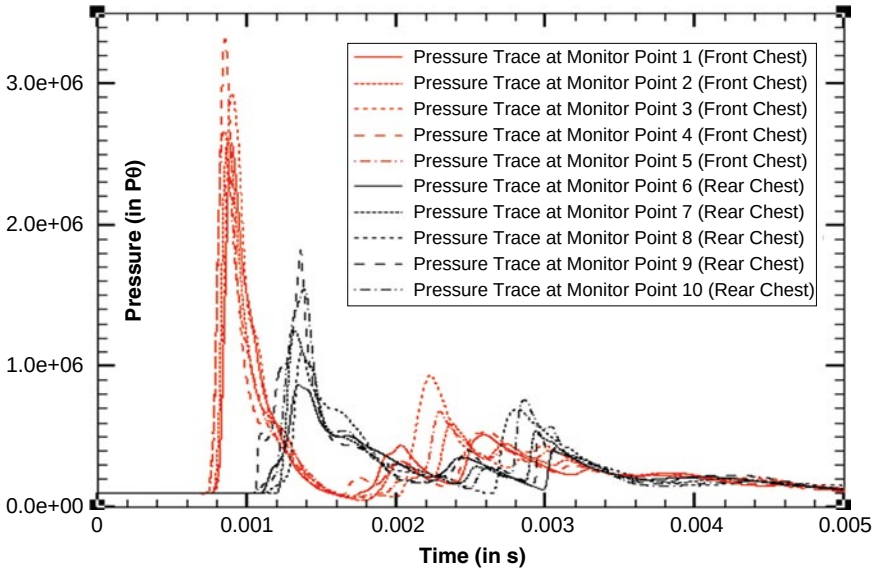

Pressure Trace at Monitor Point 1 (Front Chest)
Pressure Trace at Monitor Point 2 (Front Chest)
Pressure Trace at Monitor Point 3 (Front Chest)
Pressure Trace at Monitor Point 4 (Front Chest)
Pressure Trace at Monitor Point 5 (Front Chest)
Pressure Trace at Monitor Point 6 (Rear Chest)
Pressure Trace at Monitor Point 7 (Rear Chest)
Pressure Trace at Monitor Point 8 (Rear Chest)
Pressure Trace at Monitor Point 9 (Rear Chest)
Pressure Trace at Monitor Point 10 (Rear Chest)
Pressure (in Pa)
3.0e+06
2.0e+06
1.0e+06
0.0e+00
0
0.001
0.002
0.003
0.004
0.005
Time (in s)

FIGURE 7-14
Simulation pressure histories at 10 monitoring points on the chest of soldier for a 0.2 kg charge with the 0.25 m soldier-to-wall distance.

monitoring locations on the front chest. The figure also shows the peak pressures sustained on the back of the chest, which are due to secondary blast waves reflected from the collision of the primary blast wave with the wall behind the soldier. Smaller, secondary blast waves reverberating around the front chest area can be observed. The higher level of reverberation and "ringing" in the pressure traces on the back of the chest (compared to the reverberation and "ringing" in the pressure traces on the front of the chest) are due to the repeated reflection of waves between the back of the soldier and the walls behind the soldier.

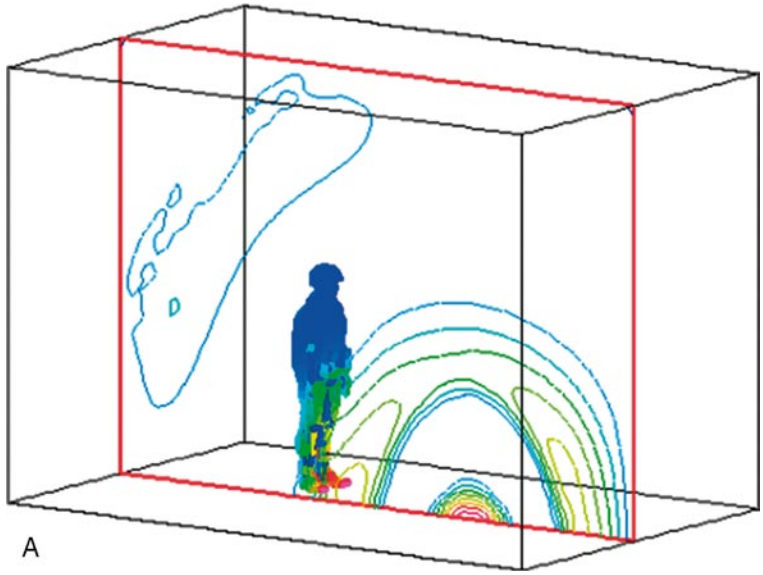
It should be noted that when a blast wave reflects from a rigid surface, the overpressure in the wave increases, possibly severalfold, so that in principle, the injury level sustained from a reflected blast wave could be higher than that from the primary blast wave. However, reflected waves also typically decay faster than incident waves, so the injury level depends on the geometric configuration, including the location and orientation of the soldier relative to the initiation site and any reflecting surfaces.

Blast Wave Induced Human Body Dynamics

In previous sections it was assumed that the soldier's body is rigid and is attached to the ground (stationary soldier position). In reality, under a

strong blast wave, the human body will be thrown up to the air, translocated, and ultimately fall back to the ground. Blast wave induced human body dynamics can be calculated using ATB tools (Cheng & Rizer 1998; Haeppee et al. 2003; Przekwas et al. 2004, 2005), which use body loads from CFD simulations, or more accurately using fully coupled CFD-ATB simulations. The latter case is computationally very challenging as it requires mesh regeneration/deformation at each time step, the coupling is nonlinear, and the problem includes disparate time scales (milliseconds for the blast wave and seconds for the human body dynamics). ATB tools treat the human body as a finite number of masses representing various body segments connected by joints. All body components have prescribed masses and moments of inertia and are connected to each other using rotational joints with prescribed rotational stiffness. The GEBOD software tools can be used to generate ATB human body models for specific anthropometric body data (Cheng et al. 1994). Figure 7-15 presents example simulation results for coupled CFD-rigid body dynamics for a soldier exposed to a spherical blast wave. During the simulation at each time step, pressure and wind shear loads were computed for various body parts corresponding to the ATB body model.

In the final computational step the ATB model was used with the time-dependent loads obtained from the CFD simulation. The objective was to understand the body dynamics in air, forces/loads/tensions on the body joints, the impact forces, and the distance traveled for various blast waves and body locations. Physical characteristics of the ATB human body model were generated using the ATB model's human body generator (GEBOD) for a 1.76 m tall, 70 kg male. The initial conditions assumed that the body is in a standing still position and the blast wave is approaching it from the front. The ATB human body model used 17 body segments connected by anatomical joints and solved the body dynamics equations for 6 degrees of freedom (6 DOF = 3 translations, 3 rotations) motion. Figure 7-16 presents example results of the ATB flexible body dynamics due to a blast explosion shown at several time instants during the body movement. The simulation results indicate that the time-scale of the human body dynamics is measured in tens to hundreds of milliseconds, whereas the blast wave propagation time is of the order of a millisecond (see Figure 7-14). The main reason for this disparate time scale is the human body inertia.



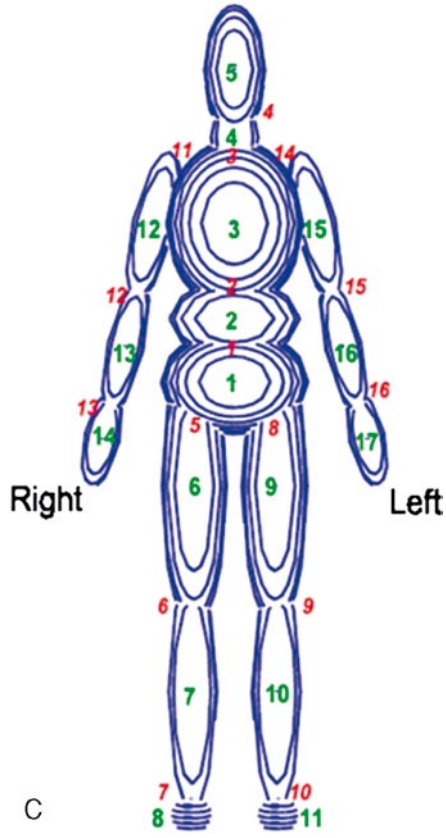


FIGURE 7-15

(A) *Selected time instant from 3D transient CFD blast wave dynamics simulation.* ***(B)*** *Segmented soldier's body used for CFD blast wave simulations and load calculation.* ***(C)*** *Articulated Total Body (ATB) model.*

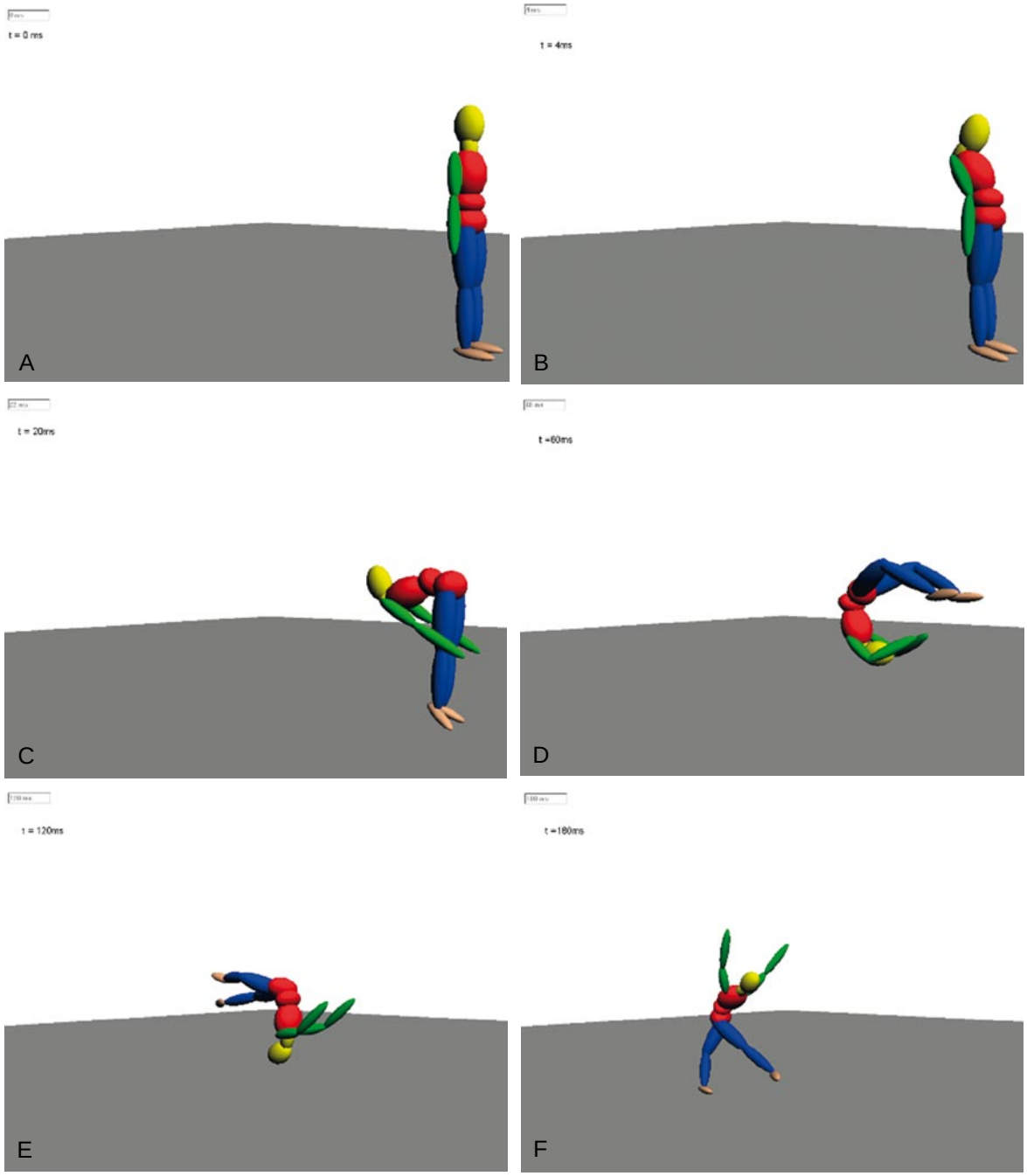


FIGURE 7-16 *Simulation of the human body dynamics and ground impact resulting from an explosion blast wave load. ATB model used CFD body loads to calculate body biodynamics.*

Continued

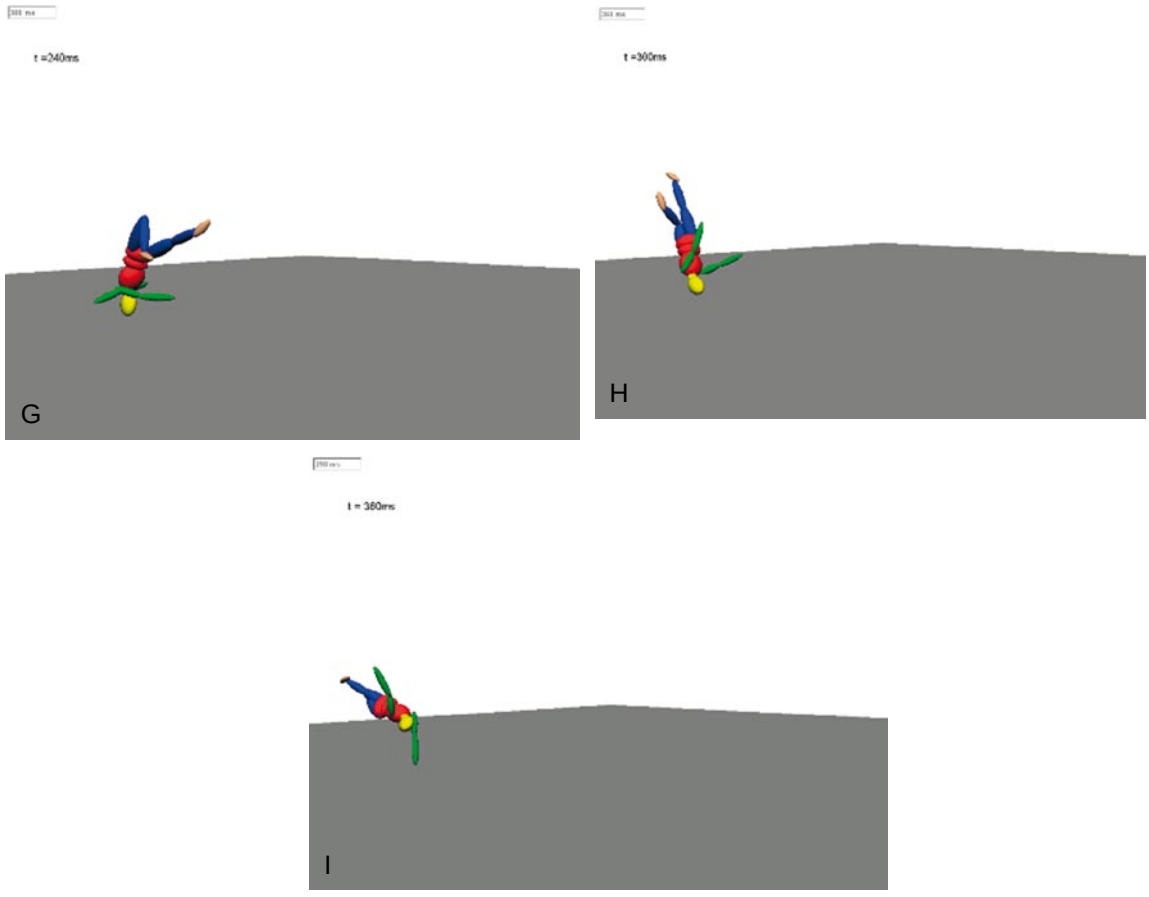


FIGURE 7-16 *Cont'd*

Simulation results indicate that the primary shock wave impacts and overpasses the body in a time scale of few milliseconds, which suggests that one can assume the body is elastic but stationary during CFD primary shock wave loading simulations. However, the conventional assumption that all the energy absorbed by the body is dissipated in the tissue is incorrect. Part of the shock wave energy will be converted to the kinetic energy of the soldier's body. After the primary wave impact, the soldier's body will start to move, and depending on the delay of secondary waves reflected from any surrounding walls, the body position and shape will be changed. These secondary waves must be accounted for in the shock wave simulations. The human body bio-dynamics simulations could prove

useful not only in better understanding of ternary blast injury mechanisms, in the design of body protective armor, but also in forensic analysis of blast explosive events.

Thorax and Lung Tissue Biomechanics and Blast Wave Injury

Injury to the lung experienced during impact or blast wave trauma can result in laceration and contusion. Laceration is induced when shrapnel cuts into the thoracic cage or when ribs are fractured and the fractured rib penetrates into the lung tissue, resulting in pneumothorax or hemothorax. Pneumothorax occurs when pleura is lacerated and air enters the pleural sac and the lung elasticity causes the lung to recoil and eventually collapse (Argyros 1997). Hemothorax occurs due to laceration of pleura or major blood vessels (e.g., intercostals) and blood is free to enter the pleural sac. Blast or impact lung contusion is generated by mechanical stress waves, which reflect, refract, and focus all over the ribcage and lungs, inducing severe stresses and strains within the lung parenchyma. Mechanical breakdown of the endothelial and epithelial barriers results in the internal flooding of the lung with interstitial fluid (edema) or blood (hematoma), both of which act as a barrier to normal oxygen and carbon dioxide exchange.

Mathematical modeling of pressure wave penetration of the thoracic/lung tissue and resultant stress/deformation biomechanics is not straightforward. Structural mechanic models of synthetic materials such as steel use well-defended material geometry and mechanical properties. Modeling ingenuity and rational assumptions are needed to formulate *in vivo* tissue biomechanics models. The biomechanics of connective and functional tissues play a fundamental role in tissue/organ physiology at all scales from macroscopic to cellular, and even to subcellular biochemical pathways. In the lung, mechanical forces directly influence function via intra- and intercellular signaling during lung morphogenesis, control of blood–air barrier and epithelial integrity, surfactant release by alveolar epithelial cells, the contractile behavior of airway smooth muscle, immune and inflammatory control, or tissue remodeling after injury (Suki et al. 2005; Fredberg & Kamm 2006). At the same time the microscopic mechanical properties of over 60 types of lung cells and the extracellular matrix have the physiological regulatory role as well as constitute the macroscopic biomechanical property of lung parenchyma. More than

anything else, the lung is a mechanical organ. During breathing, lungs experience continual mechanical loads, deformations, and stresses due to movement of the diaphragm and thoracic cavity. The cyclical expansion/contraction of alveoli results in continuous inspiration/expiration of lung gases, but also in elastic elongation/relaxation of alveolar walls covered by a thin layer of liquid surfactant and with embedded pulmonary capillaries.

Figure 7-17 presents lung anatomy at four scales, from whole body to individual alveoli. The alveolar septum walls, Figure 7-17C, experience an external force of alveolar air pressure as well as internal reaction forces due to elongation, compression, shearing, and twisting of walls. During traumatic events such as mechanical blow or blast wave impact, some of the alveolar walls experience deformations larger than the elastic limits, resulting in partial or complete septum breakup. This typically is associated with intraalveolar accumulation of proteinaceous fluids (edema) due to the vascular epithelial barrier being overstretched with transcellular and intercellular gaps, or blood (hemorrhage) due to the blood capillary breakup. Both cases result in the influx of inflammatory cells into the alveolar epithelial and surfactant layers.

In biomechanics, the macroscopic structural and mechanical properties of living tissues and organs are defined by establishing mathematical relations, called the constitutive equations, between force, deformation, stress, strain, and other variables. The material properties typically are obtained from *in vivo* or *in vitro* experimental tests. Table 7-1 presents fundamental definitions and relationships used in structures mechanics. In classical elastic solid mechanics the stress–strain relationship (Hooke's law) is linear. The constitutive equations for biological tissues are typically nonlinear and can be rate-of-strain (deformation) dependent. In contrast to elastic materials, a viscous fluid under shear stress obeys $\sigma = \eta \cdot d\varepsilon/dt$, with η as the viscosity. When the constitutive equation also characterizes the time-dependent or dynamic stress-strain properties, the tissue usually is referred to as viscoelastic. Virtually all living tissue containing water and a variety of biological macromolecules, such as collagen, elastin, and proteoglycans, behaves as a viscoelastic material (Fung 1993).

Unlike any other organ, lung parenchyma tissue consists of alveolar air pockets separated by thin septum tissue. Mechanical properties of such a gas-solid two-phase "composite" material depend on elastic properties

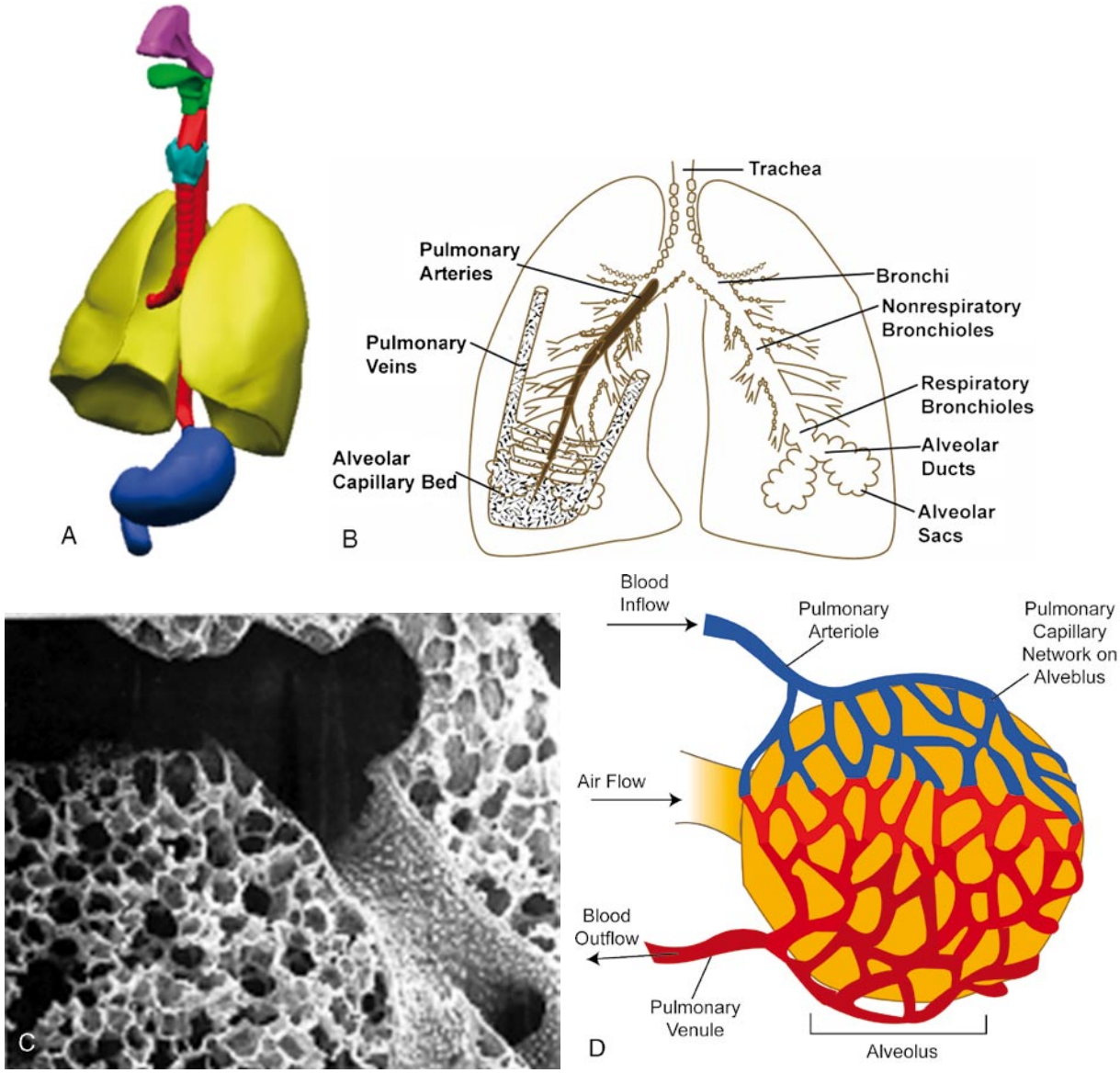


FIGURE 7-17 *Human lungs structure global and alveolar view. [LBNL Image Library—Index of LUNG_STRUCTURE] (http://imglib.lbl.gov/cgi-bin/ImgLib/makeindex?LUNG_STRUCTURE=browse)*

of alveolar walls and viscous properties of the air and surfactant and are complicated to calculate. As discussed earlier, during the lung inspiration air enters the alveoli by the pressure difference between the ambient atmosphere and pleural pressure, which is typically negative. Note that units for stress σ and pressure p are exactly the same; in fact compressive

Table 7-1 Basic Biomechanical Definitions and Constitutive Equations

Tensile/ compressive stress	Shear stress	Strain and shear strain	Hooke's law elastic stress-strain relationship	Poisson's ratio
$\sigma = F/A_0$	$\tau = F/A_0$	$\varepsilon = \Delta L/L$ $\gamma = \mathrm{tg}\theta$	$\sigma = E\varepsilon$ $\tau = G\gamma$	$\nu = \varepsilon_{lateral}/\varepsilon_{axial}$

θ is the twist angle is used as "deformation" for torsional or shear stresses definition
ΔL is the deformation (elongation of the original length L)
A_0 in stress indicates the initial area (since it changes during deformation)
E is Young's modulus or modulus of elasticity (is the slope of the stress-strain curve)
G is the shear modulus. Elastic moduli, E and G and measure the stiffness of the material
ν is the Poisson's ratio influences the speed of propagation and reflection of stress waves

stress is a pressure. Assuming local force equilibrium in the septum wall, it can be shown that the average stress acting on the lung tissue must be equal to the pleural pressure (Fredberg & Kamm 2006). The usually negative pleural pressure implies a state of tension in the lung tissues. The parenchymal tissue network transmits this tension from the pleura into the lung tissue. This distending stress is partially balanced by the surface tension forces within alveolar surfactant film. The surfactant also acts as a viscous (energy consuming) damping device. Pulmonary blood, the other fluid in the lung, also exerts pressure on the alveolar walls. The pulmonary blood pressure in capillaries is higher in the arteriolar and smaller at the venular side and larger than the alveolar air pressure. During lung inflation, the lower pleural pressure causes the lung to inflate, vascular transmural pressure to increase, and blood to accumulate in the thoracic cavity. The alveolar pressure-stress balance is essential to lung function and stability and is responsible for the ventilation-perfusion matching.

During traumatic mechanical disturbances (e.g., due to blast wave or mechanical impact) the compression/expansion pressure wave propagating through the lung parenchyma will disrupt that pressure-stress balance and result in tissue damage. The blood–gas barrier is extremely thin and breaks when it is exposed to high transmural pressures. Increase of surfactant fluids due to edema or hemorrhage will not only increase the oxygen diffusion resistance but also increase the surface tension pressure in the lung, which typically is not recognized by the medical community. The Laplace law states that the pressure difference (p_γ) acting across the gas–liquid interface is proportional to the surface tension (γ) and inversely proportional to the radius (r) of curvature of the interface: $p_\gamma = \gamma/r$. Note

that the tension in the surface film is $T_\gamma = p_\gamma{}^\star r$. During the respiration the total recoil pressure p, is the sum of p_γ and the stress (force per unit area) provided by tissue elements σ_t.

Mechanical deformations of lung tissue also have a significant effect at the cellular level, both at the epithelial and endothelial interfaces with surfactant/air and blood, respectively. For example, stretched alveolar epithelial cells will experience increased plasma membrane permeability, depolarization, and ultimately membrane rupture. Lung epithelial cells have developed defensive mechanisms and can be resealed by rapid cytosol to membrane lipid trafficking and site-directed exocytosis. In a healthy lung, fluid (water and solutes) filtered from the vascular space into the interstitium percolates through the interstitium and is cleared by the initial lymphatics. An increased permeability of the pulmonary endothelial barrier results in excessive fluid filtration and accumulation in the interstitium (interstitial edema).

From the macroscopic point of view, lung parenchyma is a mixture of a compressible gas, almost incompressible surfactant liquid and blood, and viscoelastic solid tissue. Macroscopic material properties such as density, viscosity, elastic moduli, speed of sound, and others have to be established to facilitate mathematical modeling of pressure wave propagation in lungs. Speed of sound in the lung has been studied for decades to understand blunt and blast injuries but also acoustic/ultrasonic imaging and lung injuries during ultrasonic imaging and therapeutics (e.g., extracorporeal shock wave lithotripsy) (Frizzell, O'Brien & Zachary 2003). The first reliable measurements of sound speed in lungs were published by Rice (1983). He reported that the speed of sound in air-inflated lung ranges from 30 m/sec for low air inflation to 60 m/sec for a maximally inflated lung. These values seem counterintuitive, as they are much smaller than either the speed of sound in air or water. The following mathematical derivation explains this dilemma.

The human lung can be assumed to be a two-phase porous elastic continuum, because the sound wavelength is larger than the alveoli size and alveoli do not communicate. For example, the lung has an audible frequency (f) range of 20–600 Hz and the speed of sound (c) in air is 350 m/sec. Wavelengths (λ) may be calculated as $\lambda = c/f$. Thus the range of wavelengths for the speed of sound through the lung are 350/20~17.5 m and 350/600~0.6 m—which are much bigger than the alveoli size. We can therefore average the gas and tissue properties over the volume to obtain the acoustic properties (bulk mod-

ulus K, and density ρ) of the equivalent homogeneous continuum needed to calculate the speed of sound $c^2 = K/\rho$ (Eg. 7.14). Let h be the volumetric proportion of the tissue phase and *(1–h)* the gas phase proportion:

$$h = \frac{V_T}{(V_T + V_A)} \tag{7.17}$$

where V_A is the volume of air in the lung and V_T the volume of lung tissue (0.8 L for human). The average density is given by

$$\rho = h\rho_t + (1-h)\rho_g \tag{7.18}$$

where the subscript t is for tissue and g for gas, respectively. Similarly the average bulk modulus is

$$K = \left[\frac{h}{K_t} + \frac{(1-h)}{K_g}\right]^{-1} \tag{7.19}$$

Inserting Equations (7.17) and (7.18) into the speed of sound formula Equation (7.14) and assuming an ideal gas, $K_g = \gamma^* p$, where γ is the ratio of specific heats (in air $\gamma = 1.4$) we have:

$$c = \left[\left(\frac{h}{K_t} + \frac{1-h}{\gamma \cdot p}\right)\{h\rho_t + (1-h)\rho_g\}\right]^{-1/2} \tag{7.20}$$

Assuming that $\rho_t = 1000\,kg/m^3$, $\rho_g = 1.2\,kg/m^3$, $K_t = 2.3109\,N/m^2$, air pressure $p = 10^5\,N/m^2$, and calculating h from a lung density of approximately $100\,kg/m^3$ (for transpulmonary pressure of 15 cm H_2O) the lung sound speed is approximately 55–65 m/sec, values quite close to experimental measurements (Rice 1983; Berger et al. 2005). Note that for air, $h = 0$ and $c = 348$ m/sec, and for air free tissue $h = 1$ and $c = 1{,}504$ m/sec. Note also that the auditable acoustic wavelengths propagating in lungs, $\lambda = c/f$, are $60/20 = 3$ m to $60/600 = 0.1$ m, which are much smaller than in other tissues such as the heart or brain. It should also be pointed out that at high frequency (1–5 kHz) the speed of sound in lungs is much higher, frequency dependent, and the wave attenuation (energy absorption) rapidly increases with the frequency and inflation volume. In collapsed lung tissue, even high frequencies (5 kHz) have relatively small attenuation (Berger et al. 2005).

A blast wave impact on the thoracic cavity will most likely create a full range of frequencies, and those associated with the initial shock front penetration will be rapidly absorbed in the lung tissue causing localized injury. Longer wavelengths will easily propagate to the opposite side of the thoracic cavity and partially rebound back. Recent studies of ultrasonic lung hemor-

rhagic injury demonstrated that high frequency waves are absorbed locally near the sound source and that the hemorrhage is proportional to total energy exposure and are not caused by the inertial cavitation (Frizzell et al. 2003). As the propagating blast wave passes over the thoracic wall it will cause both *stress waves* and *shear waves* within the thoracic tissues and in the lung parenchyma. The stress waves, longitudinal pressure waves, travel at or slightly faster than the speed of sound, but are of high amplitude. The potential mechanical lung injury mechanisms may involve:

- Pressure differentials across the alveolar septa.
- Wave reflection at the interface between two media of different acoustic impedance (e.g., alveolar tissue and air). Acoustic impedance is the product of the density and the speed of sound in that medium. Part of the wave is transmitted and the remainder is reflected as a tension wave with disruption at the interface, a phenomenon known as *spalling*.
- A stress wave that may compress an alveolar gas causing collapse, followed by a forceful reexpansion that damages the alveolar wall.

Shear waves are low-velocity transverse waves, resulting from transient deformation of the body wall. It is generally accepted that shear waves are less destructive in lungs but cause significant injury in other organs such as brain, heart, abdominal viscera, mesenteries, and the large bowel.

Previous studies of blast injury and high-velocity impacts (Fung et al. 1998; Bush & Challener 1988; Cooper 1991) discussed the importance of proper resolution of pressure wave dynamics in the lung. The experimental studies of Yen et al. (1998), Fung (1990), and Copper (1991) have shown that the velocity and acceleration of the thoracic wall (or the lung surface) under the impact point correlate well with the occurrence of lesions. Stuhmiller et al. (1996) and Copper (1991) have considered the history of the pressure wave generated in the thorax as an indicator for impact lethality. They have shown that waves rising slowly to their peak value have less lethality than those characterized by a fast rising shock front. These and ultrasonic injury experiments strongly indicate that the hemorrhage and edema in the lung are due to the high-frequency damage mechanism.

Reduced Models of Blast Wave Tissue Biomechanics and Injury

Compact, or reduced, modeling approaches offer fundamental and approximate, yet instructive ways to analyze biomechanics of biological tissues.

Typically biological tissue is treated as a viscoelastic material integrating both elastic solid (restorative force property) and viscous fluid (dampening property) behavior. Elastic materials store all the energy as deformation, and viscoelastic materials store part and dissipate the rest of the energy. The ability to dissipate energy is one of the main reasons for using viscoelastic materials for any application to analyze the shock wave propagation and absorption in tissue.

Mathematical models for such tissues use mechanical analogues of mass-spring-dashpot and force elements. Figure 7-18 presents the basic building blocks of biomechanical analogues of viscoelastic tissue models. Connecting an elastic spring and a viscous damper in series yields the Maxwell material model, their parallel connection yields Voigt material model, and parallel combination of the Maxwell and spring models form the Kelvin model (also known as the three-parameter viscoelastic solid) (Fung 1993).

The Hookean spring model provides a linear relation between the applied force F and the resultant spring deformation u, in the form $F = -ku$, where k is the spring constant (or elastic constant). In the stress-strain form the Hookean spring model is expressed as $\sigma_s = E\varepsilon_s$ where σ is the applied stress (force per unit area), E is the Young's modulus (equivalent to spring constant, k) of the material, and ε is the strain (relative deformation). In the Newtonian dashpot model the force F is linearly related to the displacement rate v (or velocity $v = \dot{u} = du/dt$) in the form $F = D\dot{u}$, where D is the damping coefficient equivalent to viscosity η of the dashpot dampening "fluid." In the stress-strain form the Newtonian dashpot model relates the applied stress with the strain rate: $\sigma_d = \eta(d\varepsilon/dt)$. More complex biomechanical models can be created by combing these two basic components in series (Maxwell model), in parallel (Voigt model), or in more complex networks (e.g., Kelvin model). The mathematical formulas for the Maxwell and Voigt models in force-deformation and stress-strain forms are:

$$\text{Maxwell model:} \qquad \dot{u} = \frac{\dot{F}}{k} + \frac{F}{D} \qquad \text{or} \qquad \dot{\varepsilon} = \frac{\dot{\sigma}}{E} + \frac{\sigma}{\eta} \qquad (7.21)$$

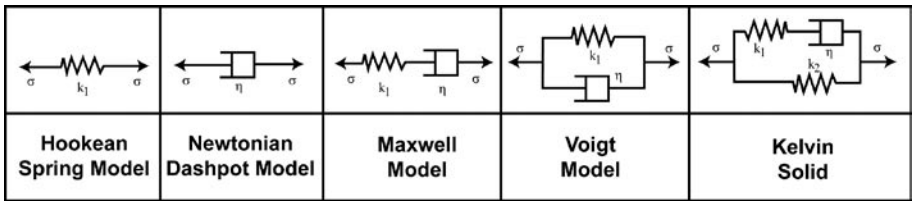


FIGURE 7-18
Basic building blocks of viscoelastic tissue models using mechanical analogues.

$$\text{Voigt model:} \qquad F = ku + D\dot{u} \quad \text{or} \quad \sigma = E\varepsilon + \eta\dot{\varepsilon} \qquad (7.22)$$

where a dot above the variable denotes a time derivative. Note that by normalizing the force, F, by area and the displacement, u, by length, we can convert the force-deformation to the stress-strain form. Noting that $\sigma = F/A$ and $\varepsilon = u/L$ we can express force-deformation to the stress-strain formulation:

$$\frac{F}{A} = \frac{L}{A}k\frac{u}{L} + \frac{L}{A}D\frac{\dot{u}}{L} \quad \text{or} \quad \sigma = E\varepsilon + \eta\dot{u}$$

The Maxwell model cannot account for a retarded elastic response so it can be used only for small deformations, whereas the Voigt model does not describe stress relaxation. Both models are characterized by single relaxation times—a spectrum of relaxation times would provide a better description. That can be achieved, for example, by connecting several Maxwell models in parallel or Voigt models in series. Once such a model is developed, its parameters, E or k and η or D for each element, have to be obtained from experiments.

The first application of compact models for the thoracic biomechanics and blunt impact injury was proposed by Lobdell et al. (1973). In his model, schematically depicted in Figure 7-19A, several springs, masses, and dampers have been combined to represent thoracic anatomical structures and an impact mass (m_1). Mass m_2 represents the sternum and the anterior part of the rib cage and mass m_3 represents the thoracic cavity including vertebral column and the posterior part of the rib structure. Spring k_{12} represents the elasticity of the skin and the protective clothing. The sternum and the thoracic masses are connected through parallel Voigt (k_{23}, η_{23}) and Maxwell (kve_{23}, ηve_{23}) models where the spring k_{23} represents the elasticity of the rib cage and attached viscera, the damper η_{23} represents the lung air and pulmonary blood and the Maxwellian spring-mass parameters represent the viscoelastic thoracic muscle tissue. This model was used as the basis for developing the thoracic components of the Hybrid III dummy.

The Lobdell model was further extended by Viano (1978, Viano & Lau 1988), shown in Figure 7-19B, by including a secondary spring, k_{23s}, to represent the bilinear increase of the thoracic stiffness at high levels of compression. Viano's model also included the computation of kinetic energy, power, and momentum of the masses, and the energy absorbed in springs and dissipated in dampers. He extensively studied the influence of protective effects of the energy absorbing materials in front and side impacts.

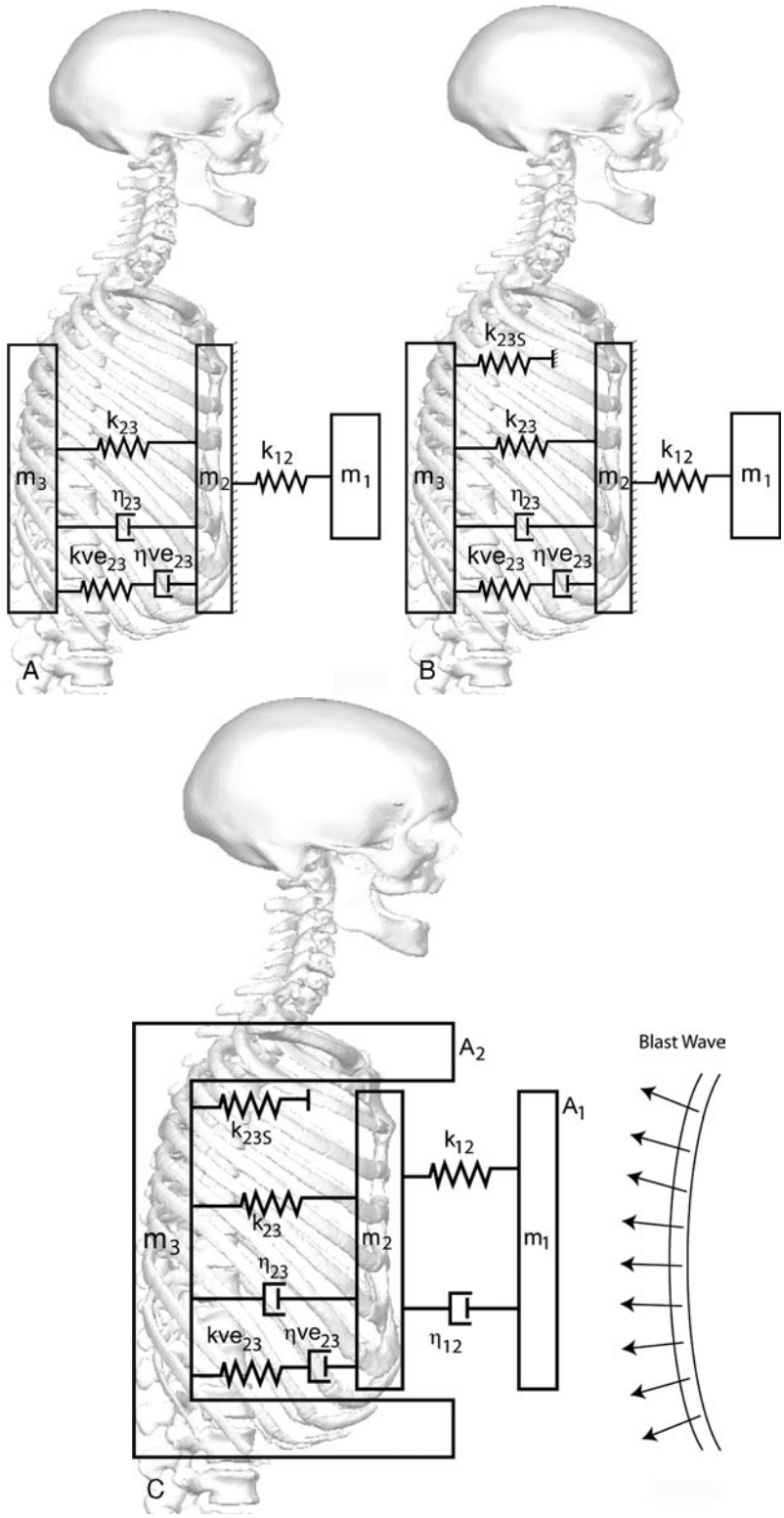


FIGURE 7-19

Spring-Mass-Dashpot compact model of thoracic biomechanics and impact injury (based on Lobdell et al. 1973; Viano 1978; Viano & Lau 1988; Stuhmiller et al. 1996).

Compact models also have been used in thoracic injury biomechanics during a blast wave impact (Stuhmiller et al. 1996, 1999; Axelsson & Yelverton 1996; Grimal, Watzky & Naili 2002). To account for viscous compression and dissipation of the shock wave around the body, Stuhmiler modified the Lobdell-Viano model by replacing the k_{12} spring with a Voigt model. In the blast wave impact the thoracic loading with mass m_1 is replaced by calculating the time-dependent shock wave pressure loads to the thorax. The compact models incorporating mass, spring, and damping device elements can also be expressed in a general Newton's second law form:

$$M\frac{dv}{dt} + D \cdot v + k(u - u_0) = F_{ext} \tag{7.23}$$

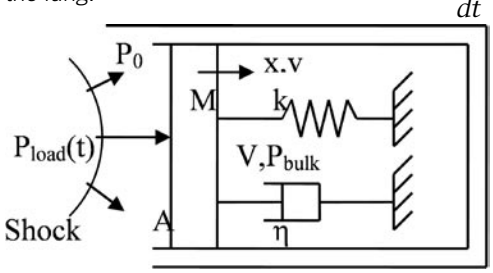
where M is the tissue mass, v is tissue velocity, u deformation, and F_{ext} external force (e.g., due to blast wave load). Probably the most fundamental human lung injury model has been developed by Stuhmiller in collaboration with the Army WRAIR, MRMC, and other DoD organizations (Stuhmiller 1996, 1997, 1999). The model and data have been integrated into an "INJURY" software framework. The model assumes that the lung behaves as compressible gas and uses the Landau-Lifshitz correlation, which relates the pressure wave in a compressible gas to the piston speed (see Figure 7-20):

$$p(t) = p_0 \cdot \left(1 + \frac{1}{2}(\gamma - 1)\frac{v}{c_0}\right)^{\frac{2\gamma}{\gamma - 1}} \tag{7.24}$$

where $p_{0,}$ $\rho_{0,}$ and c_0 are the pressure, density, and speed of sound in the undisturbed lung, v is the piston velocity, and γ is the ratio of specific heats. Using the chest velocity-pressure wave relationship, Stuhmiller constructed the formula for the amount of energy delivered to the lung, assuming that the thoracic response to blast is dominated by inertia and external pressure loading, p_{load}. By ignoring the stress in the rib structure and internal wave reflections he could write in general Newton's second law as:

$$m\frac{dv}{dt} = p_{load}(t) - p_0 \cdot \left(1 + \frac{1}{2}(\gamma - 1)\frac{v}{c_0}\right)^{\frac{2\gamma}{\gamma - 1}} - \frac{p_0 L}{L - x} \tag{7.25}$$

FIGURE 7-20
Generalized pleural dynamics compact model coupling external load, thorax wall, and compressible air in the lung.



where v is the chest wall velocity, x is the displacement, m is the chess mass per unit wall area, and L is the lung volume per unit of chest wall area. Having p_{load} one can calculate the chest wall speed v. Finally, the normalized work, $W^{\star}$, defined as the total

work done to produce the wave in the lung per unit lung volume, V, and unit pressure p_0, can be computed using velocity v from Eq. (7.24) as:

$$W^* = \frac{W}{p_0 V} = \frac{1}{p_0 L}\int_0^\infty \rho_0 c_0 v^2 dt \qquad (7.26)$$

Even though the model (Eqs. 7.23–7.25) does not compute the local strain in the lung tissue, it provides a global injury parameter, the work dissipated in the lung tissue. When calibrated on selected experimental data the model correlates well with the rest of experimental data as shown in Figure 7-21.

Axelsson & Yelverton (1996) developed a compact lung model consisting of a two-chamber spring-mass system, "two-lung model," and applied complex overpressure shock wave forms based on experimental observations. Complex blast waves typically consist of multiple shocks with variable frequency content and intensity that may be superimposed on a slow rising quasi-static pressure pulse. For each of the lungs the two-lung model uses spring-mass model coupling the chest wall response (displacement, velocity, and acceleration) and intrathoracic pressure. Figure 7-20 presents the spring mass model for one of the lungs. The model has been verified on sheep and used for modeling of human lungs. The model predicts that as the pressure goes up in the lung cavity, the lung becomes stiffer and its spring constant increases, subsequently increasing the "resonance" frequency. For example, for sinusoidal pulse loads

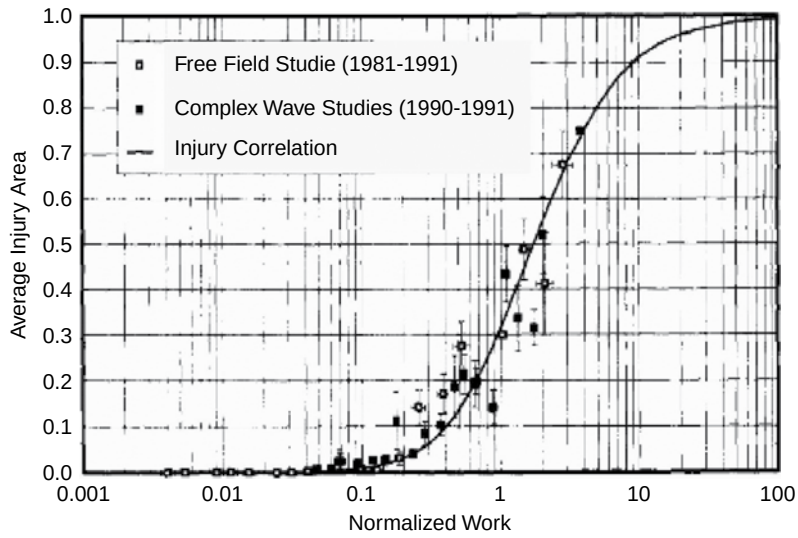


FIGURE 7-21
Correlation of degree of lung injury with normalized work. Experimental data (points) and semi-empirical correlation (curve) (Stuhmiller et al. 1996).

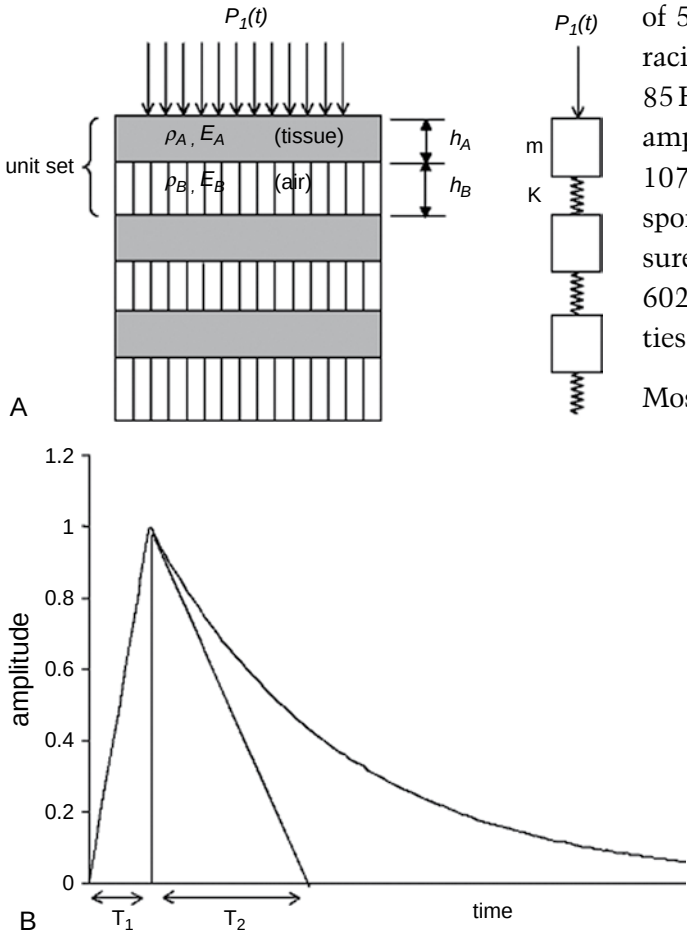


FIGURE 7-22

1D model of lung parenchyma with weakly-coupled bi-periodic layered media and the equivalent mass–spring chain ***(A)*** *and the pulse pressure loading* ***(B)*** *(Grimal 2002).*

of 50 and 200 kPa, the maximal intrathoracic pressures will be reached at 50 and 85 Hz. For step waves of 50 and 200 kPa amplitude, the resonance frequencies are 107 and 206 Hz, respectively. The corresponding maximal intrathoracic overpressures for these step wave loads are 80 and 602 kPa with respective chest wall velocities of 2.6 and 9.1 m/sec.

Most of the compact models assume the lung as an isotropic and homogeneous medium and use either purely linear elastic Hooke's or nonlinear elastic constitutive law. Further, lumped parameter models do not simulate propagation of waves in lung tissue. Grimal et al. (2002) proposed a 1D inhomogeneous two-phase succession of air pockets and a solid tissue model of the lung parenchyma (see Figure 7-22A). The lung model was loaded with a pressure pulse typical to blast waves with a rapid pressure rise during $t < T_1$, followed by an exponential decay $p_1(t) = \exp[-(t-T_1)/T_2]$, as shown in Figure 7-22B. The lung parenchyma model has been used to answer several questions including:

- Whether the foam-like structure of the lung is likely to distort the pressure wave history, and when the homogeneous medium assumption is valid
- The influence of the dimensions of the lung structure (that vary between mammalian species used in the experiments) on injury thresholds
- The generation of transeptal pressure differences for different impact characteristics

Equations of motion for the semi-infinite mass–spring chain, Figure 7-22A, excited at its end, can be written in terms of axial displacement u_n of each mass m as,

$m\ddot{u}_1 = p_1(t) - K(u_1 - u_2)$ for n = 1 (first mass loaded by external pressure) and

$$m\ddot{u}_n = K(u_{n-1} - u_n) - K(u_n - u_{n+1}) \qquad \text{for n} > 1 \tag{7.27}$$

where u is the deformation, double dot means second time derivative of u (i.e., acceleration), and $p(t)$ is the blast load on the chest wall. Note that the pressure on the n^{th} tissue block is

$$p_n = K(u_{n-1} - u_n) \tag{7.28}$$

The equivalent parameters m and K of the discrete system are derived from the properties of the continuous media:

$$m = \rho_A h_A + \rho_B h_B \tag{7.29}$$

$$K = \left(\frac{h_A}{E_A} + \frac{h_B}{E_B} \right)^{-1} \tag{7.30}$$

where ρ is the density and E is elastic Young modulus.

Figure 7-23 presents predicted time histories of pressure at several distances from the impact point for two pressure pulses, a slower and a faster pulse, with the expectation that the faster the rise, the wider the frequency spectrum. The model uses the following properties for the lung tissue:

$$E_A = 2.2e^9 \text{ Pa}, \qquad \rho_A = 1000\,\text{kg/m}^3, \qquad h_A = 5\,\mu\text{m}$$
$$E_B = 141e^3 \text{ Pa}, \qquad \rho_B = 1.11\,\text{kg/m}^3, \qquad h_B = 360\,\mu\text{m}$$

Frequency analysis indicates that each individual frequency travels at a specific velocity.

Comparison of simulation results shown in Figure 7-23 shows that:

- The maximum of $p(t)$ stays almost constant along the stack for Pulse 1 while it decreases significantly for Pulse 2
- The maximum slope of $p(t)$ decreases significantly and the discontinuity in the derivative of the pulse at $t = 0$ disappears
- The oscillations increase with the distance from the top of the stack

An even more elaborate distributed 1D model of blast wave propagation in the lung recently has been proposed by D'yachenko & Manyuhin (2006). The model includes the following four phases in continuum medium: (1) the gas filled alveoli, (2) tissue structures (alveolar walls, fine airways and blood vessels with blood), (3) the entrance to the large airways, and (4) the entrance to the large blood vessels. The governing equations of the parenchyma are modeled as a multiphase medium.

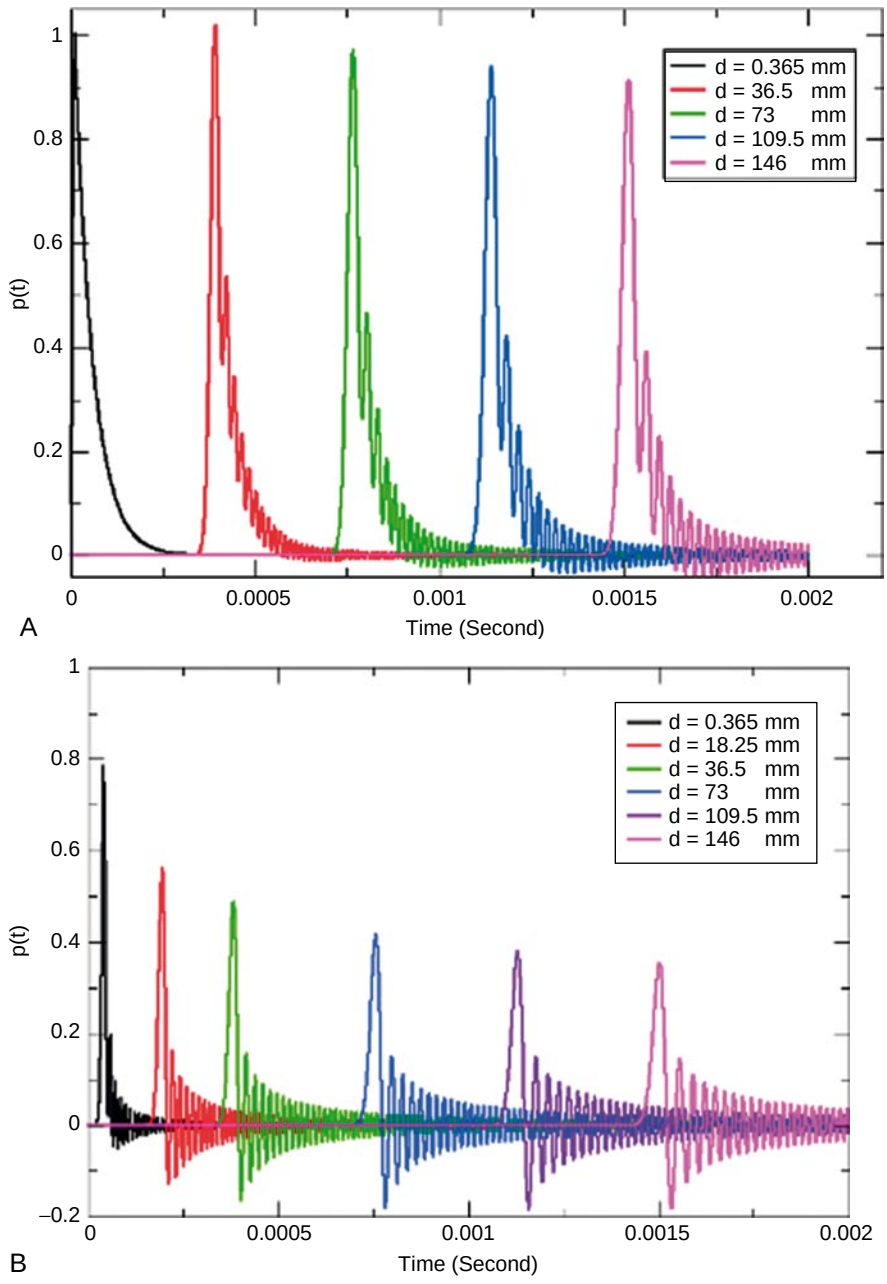


FIGURE 7-23

Time histories of the pressure at several distances d (mm) from the impact point (Grimal et al. 2002 test case). ***(A)*** *Slower Pulse 1. p=exp [-(t-10^{-5})/5*10^{-5}].* ***(B)*** *Faster Pulse 2. p=exp[-(t-10^{-6})/ 1*10^{-5}].*

Multidimensional Modeling of Lung Tissue Biomechanics

Detailed understanding of impact and blast wave tissue biomechanics, pressure wave propagation in the thoracic cavity, and lung injury location and severity can be analyzed using multidimensional models. Such models solve partial differential equations on 2D or 3D computational

grids located within the thorax tissue and lung, and for blast waves around the human body (see Figure 7-7B). A complete blast wave primary injury model should involve the fully coupled solution of external gas dynamics equations (typically solved by Computational Fluid Dynamics [CFD] methods), human body dynamics and thoracic cavity tissue stress, deformation biomechanics solved by Finite Element Methods (FEM), and highly viscoelastic gas-solid mechanics of lung parenchyma. Solution of such Fluid-Structures-Interaction (FSI) problems is very challenging, and reliable computational methods for 3D transient FSI problems are beginning to emerge (Dettmer & Peric 2006; Guruswamy 2006). Multidimensional modeling of blunt or blast lung injury has been conducted using various simplifying assumptions in lung geometry representation and in mathematical biomechanics equations. This section briefly describes general structure biomechanics models, FSI methods, and simplification techniques.

Fundamental equations of continuum mechanics are common for both fluid and solid mechanics. The solid body and fluid mechanics actually share the same governing equations, and differ only in constitutive relations. The governing partial differential equation (PDE) of motion for both a fluid and a solid are the momentum equations:

$$\rho \dot{v}_i = \sigma_{ij,j} + f_i \tag{7.31}$$

where ρ is the density, v_i is the velocity, σ_{ij} is the stress tensor, f_i is the internal body force, a superscript dot designates a total derivative, and a comma is for a partial derivative with respect to the following variable. Repeated indices denote summation over the appropriate range. To close the system in Equation (7.30), the information about the response of a particular material to an applied force is necessary. Following, a compressible gas and elastic solid are used as examples of fluid and solid materials.

Constitutive equations for fluid:

- Equation of state for compressible gas:

$$\rho = \frac{p}{RT} \tag{7.32}$$

where p is the pressure, R is universal gas constant, and T is absolute temperature

- Constitutive stress and rate of deformation relation for fluid (Stoke's law):

$$\sigma_{ij} = \mu\left(v_{i,j} + v_{j,i}\right) - \frac{2}{3}\mu\delta_{ij}v_{k,k} - p\delta_{ij} \tag{7.33}$$

where σ_{ij} is the stress tensor, v is the fluid velocity, μ is the dynamic viscosity, and δ is the Kronecker delta.

Constitutive equations for the elastic solid:

- Stress-strain (deformation) equation (Hooke's law):

$$\sigma_{ij} = \eta\left(u_{i,j} + u_{j,i}\right) + \lambda\delta_{ij}u_{k,k} \tag{7.34}$$

where η and λ are the Lame constants, u_i is the displacement vector related to velocity by simple time derivative:

$$v_i = \dot{u}_i \tag{7.35}$$

Note that in the fluid, the stress is expressed in terms of velocity v, whereas in the solid it is expressed in terms of displacement, u. This system of equations describes both fluid flow and solid biomechanics. Historically, however, both disciplines have been conveniently divided into two. As a result, problems involving FSI typically are treated separately, in a decoupled manner, and often using completely different solution techniques, such as the finite volume method (FVM) for fluid flow and FEM for structures mechanics.

For FSI problems, one needs to specify interface boundary conditions. It is required that the displacement, velocity, and stress are continuous; that is,

$$\left(u_i\right)_s = \left(u_i\right)_f; \quad \left(v_i\right)_s = \left(v_i\right)_s; \quad \begin{matrix} \left(\left(\sigma_{ij}\right)_n\right)_s = \left(\left(\sigma_{ij}\right)_n\right)_f \\ \left(\left(\sigma_{ij}\right)_\tau\right)_s = \left(\left(\sigma_{ij}\right)_\tau\right)_f \end{matrix} \tag{7.36}$$

with subscript s and f representing solid and fluid domains, respectively. Here n and τ are the normal and tangential directions of the solid-fluid interface. The fluid and structure equations are coupled by a velocity compatibility and equilibrium of tractions conditions:

$$\begin{aligned} \dot{u} &= \mathrm{v} \\ \sigma_S \cdot n &= -p \cdot n + \sigma_F \cdot n \end{aligned} \tag{7.37}$$

where u is the deformation, v is the velocity of the fluid, p its pressure field, σ_S and σ_F are the structure stress tensor and the fluid viscous stress tensor.

When the solid body deforms, the fluid computational grid points on the solid surface will move with the solid, while the rest of the fluid volume mesh has to be deformed (remeshed) around the solid body. Effectively the fluid equations have to be solved on a moving deforming mesh and mesh movement has to be computed at each time step. Figure 7-24 explains the remeshing procedure. The equations governing the structures and fluid dynamic mesh deformations are coupled by the continuity conditions,

$$x = u \qquad \text{and} \qquad \dot{x} = \dot{u} \tag{7.38}$$

The structures mechanics equations typically are solved using FEM method. As in CFD, a mesh is generated within the solid body and continuous functions (deformation, velocity, stress) are replaced by their discrete values at the nodes of each element. The PDEs are approximated with interpolation on each element resulting in a large set of nonlinear algebraic equations, which can be solved either implicitly (full equation set at once) or explicitly (for each mesh node at each time step). For transient biomechanics problems, such as blast wave impact, a large number of fine meshes and very small time steps typically are needed. Such problems can be solved only by using explicit schemes, which are constrained by time step limitations. An implicit scheme would require a very computationally expensive large nonsymmetric matrix inversion at each time step. FSI problems contain additional complications and nonlinearities involved in fluid pressure-structure deformation constraints, moving CFD mesh, and remeshing.

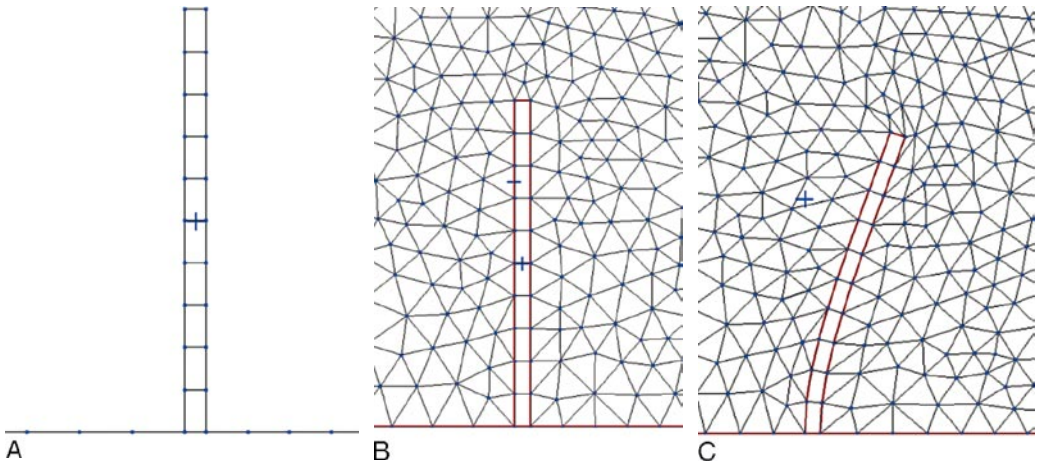


FIGURE 7-24
Remeshing procedure of fluid mesh for a fluid-structures-interaction problem. ***(A)*** *FEM mesh in the undeformed solid.* ***(B)*** *Undeformed solid mesh and the original fluid volume unstructured mesh.* ***(C)*** *"Remeshed" fluid domain conforming to deformed solid.*

Coupling between fluid and structures can be addressed in two ways. In a *weakly coupled* method, fluid and solid equations are solved separately and only at the beginning of each time step are loads from fluids and deformations from solids exchanged. This commonly is done because of problem complexity and because there are very few fully coupled FSI solvers available. A *fully coupled* method is computationally much more complex, but offers good numerical accuracy, stability, and robustness. The next section presents example blast wave human body biomechanics simulation results using both methods.

BLAST WAVE LUNG INJURY MODEL

Models of Blunt and Blast Wave Primary Lung Injury

Finite Element Methods (FEM) have been used almost from the very beginning of their invention in mid-1960s, by Zienkiewicz at the University of Swansea in Wales and by Taylor at the University of California in Berkeley (Zienkiewicz & Taylor 2000). Three dimensional FEM models of thoracic cavity biomechanics and lung injury have been under continual development, primarily driven by automotive crash safety demands (Wang 1995; Deng et al. 1999; Iwamoto et al. 2002; Behr et al. 2003; Haeppee et al. 2003; Ruan et al. 2003, 2005; Forbes 2005), and to a lesser degree by interest in blast wave (Stuhmiller et al. 1996, 1999) and behind armor body injury (Grimal et al. 2004; Roberts et al. 2006). In spite of differences in thoracic wall loading patterns and time scales involved in kinetic and blast wave impacts, the underlying tissue biomechanics and the computational modeling approaches are very similar.

FEM models of human body biomechanics have been investigated for over three decades, but the detailed human anatomy based resolution models appeared in the mid-1990s after the Visible Human data became available (Spitzer et al. 1996). Wang (1995) at Wayne State University, Detroit, MI., developed a fiftieth percentile male human thorax FEM model based on the Visible Human dataset. The model includes the entire musculoskeletal structure, thoracic wall, rib cage, spinal column, and thoracic soft tissue internal organs: the lungs, heart, aorta, vena cava, and primary pulmonary arteries and veins. Wang's (1995) FEM model assumed elastic properties for bones and viscoelastic properties for the muscular tissue and organs. In the early FEM human body models, individual organs of the thoracic cavity and the abdomen were not accurately modeled, but generally were represented

by volume fillers with material properties obtained from cadaver impact test data (Lizee et al. 1998). As the importance of mathematical modeling of human safety became clear, automotive firms began developing their own human body models. TNO Automotive, Delft, Netherlands, has developed the MADYMO FEM based human body biomechanics commercial software (Haeppee et al. 2003). Toyota developed the THUMS (Total Human Model for Safety) human body model with high fidelity FEM resolution of thoracic tissues (Iwamoto et al. 2002). A European automotive consortium developed HUMOS (Human Model for Safety) human body FEM model (Behr et al. 2003) and Ford Motor Company developed a detailed full human body model for the prediction of human thoracic impact responses and injuries (Ruan et al. 2003, 2005). The commercial human body models made improvements to geometry, articulation, and internal organs, and biomechanical material properties. Those models have been tested and validated against cadaver and physical surrogate impact test datasets, including tests on the head, thorax, abdomen, hip, and lower extremities. Car crash FEM models still have several limitations in anatomical resolution of organs, the vascular system, tissue interactions during deformation, treatment of hollow and air-filled organs (e.g., lungs), material properties of *in vivo* organs, and the complete lack of physiology.

High fidelity FEM human body biomechanics models also have been used for military applications to study ballistic impact on a human thorax, injury mechanisms, and efficiency of protective armor. Jolly and Young (2000), at the Naval Postgraduate School, developed a FEM human thorax model that included elastic skeletal and viscoelastic tissue structure properties to study bullet impact to the human thorax and ballistic protection of the body armor. Accurate modeling of ribs in thoracic FEM biomechanics simulations is computationally very intensive, as it requires a large number of grid cells. Niu et al. (2007) have developed a novel, computationally efficient inhomogeneous FEM beam model for ribs. He has validated the model and then used it to study thoracic impact biomechanics on a 3D FEM model of a swine. In a recent study, Roberts et al. (2006) developed both a computational FEM model and a physical surrogate model of a human torso to study nonpenetrating ballistic impact. The Human Torso Finite Element Model (HTFEM) included the thoracic skeletal structure muscle tissue and major organs. The skeletal structure (ribs, sternum, cartilage, and vertebral column)

was assumed to be linear-elastic, whereas internal organs (heart, liver, lungs, and stomach), mediastinum, muscle, tissue, and skin were modeled as viscoelastic. Figure 7-25 shows the meshed components of the computational model and the integrated human torso constructed of 245,000 solid linear tetrahedral and triangle shell elements.

The instrumented physical surrogate torso was constructed using biosimulant materials and anthropometry to match the HTFEM model. To analyze the performance of ballistic protective armor, both computational and surrogate models were outfitted with the National Institute of Justice (NIJ) soft armor vests. Several ballistic tests targeting the heart and liver were conducted, measuring heart, liver, and stomach pressure and sternum acceleration. Corresponding FEM simulations were performed with the LS DYNA FEM code using the explicit integration scheme. Figure 7-26 presents computed pressure fields on the soft vest and on thoracic organs in response to a 9 mm bullet impacting the middle of the sternum at a velocity of 430 m/sec. Both experimental and modeling results showed that the pressures in organs near the impact point were higher for impact over the soft organs (liver) than over hard tissue (bone). Comparison between the experimental and computational results showed very good agreement for pressure response near the point of impact and poorer at locations further away from the point of impact. The discrepancy could be attributed to the directional sensitivity of the piezoelectric pressure sensors as well as assumptions in tissue material properties and interorgan contact treatment in the FEM model.

High-speed ballistic impact of a high caliber rifle projectile on a human torso protected by modern ceramic composite armor creates strong pressure waves propagating from the area of impact (being the armor plate) into the thoracic tissue and lungs. Grimal et al. (2004) conducted FEM simulations of high-speed blunt impact on the thorax and the resultant primary pressure wave propagation in the thoracic tissue and lungs. His very simplified three layer (muscle, bone, lung) 3D FEM model included only a small part of the thoracic wall, consisting of an $8 \times 8 \times 4$ cm box meshed with 83,780 isotropic linear elastic brick elements. Blunt impact loading, derived from experimental measurements, was introduced as an idealized time dependent pressure boundary condition. The objective of the study was to understand the formation of a steep-front pressure pulse at the idealized point of impact, its propagation through the thoracic and lung tissue, and

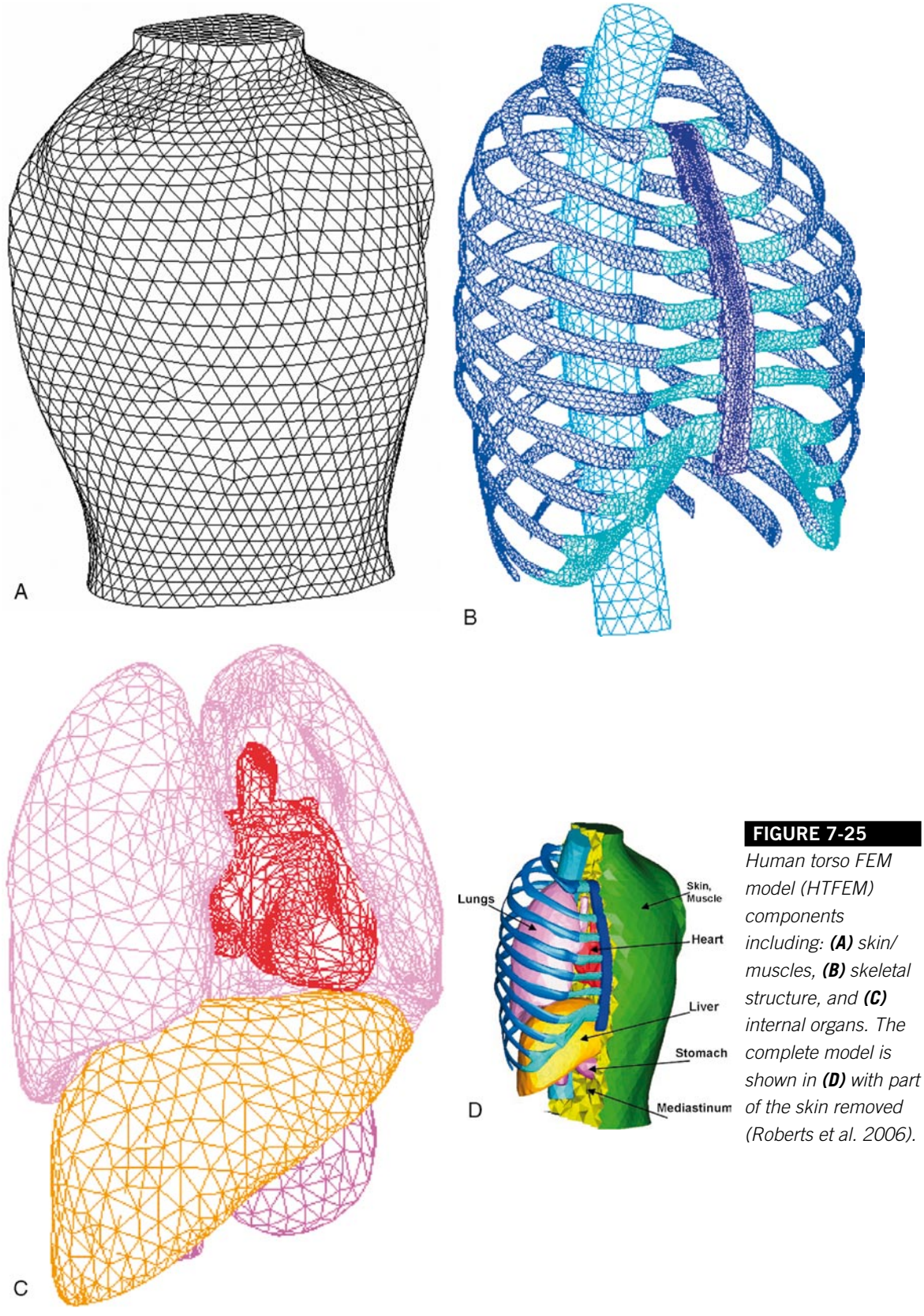


FIGURE 7-25

*Human torso FEM model (HTFEM) components including: **(A)** skin/muscles, **(B)** skeletal structure, and **(C)** internal organs. The complete model is shown in **(D)** with part of the skin removed (Roberts et al. 2006).*

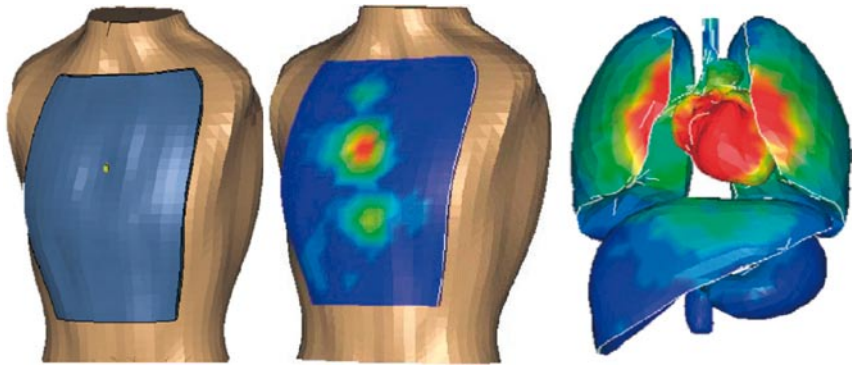


FIGURE 7-26
Computed pressures fields on the soft vest and on thoracic organs in response to a 9 mm bullet impacting the middle of the sternum at a speed of 430 m/sec (Roberts et al. 2006).

transmission of impact energy into the lung. When a high-velocity projectile (about 800 m/sec) is stopped by rigid body armor, the propagation time of the pressure wave into the lung tissue is in the range 100 to 300 μs. The time history of computed tissue pressure waves shows a steep wave front followed by an exponential decay. The simulation results showed that the predicted lung surface velocity (of about 10 m/sec) using the elastic model is smaller than the equivalent mass rigid body model and that it is much smaller than the lung tissue sound speed (approx 40 m/sec).

Velocity and acceleration of the thoracic wall have been identified as major lung risk injury parameters. Experimental and computational studies of high-velocity thoracic impacts and blast wave loadings have shown that the rapid motion of the chest wall can create a localized pressure wave in the lung parenchyma that correlates with the location of hemorrhage and edema lesions (Fung et al. 1988; Cooper et al. 1991, 1996; Stuhmiller et al. 1988, 1996). In particular, the supersonic propagation speed of blast waves results in very fast chest wall pressure loads. Experimental and mathematical modeling studies of blast lung injury have been conducted at the Army MRDC, WRAIR, and by Jaycor for over two decades (Chuong & Stuhmiller 1985; Stuhmiller et al. 1999; Elsayed & Gorbunov 2003; Gorbunov et al. 2005) with the goals of understanding the primary and secondary blast lung injury mechanisms, to develop mathematical models, and to establish injury criteria. The experimental animal blast injury data were used by Jaycor to calibrate and validate both FEM and compact models of blast lung injury (Stuhmiller et al. 1999).

The first high-fidelity model of lung blast injury was developed by Stuhmiller et al. (1988). He constructed an anatomy-based 3D FEM model of a sheep thorax and conducted a modeling study of thorax biomechanics in response to blast events. This model was divided into groups of solid elements representing the lungs, omasum, small intestine, rumen, and large intestine. The material properties in the model were assumed to be linear-viscoelastic. Due to computer limitations, the FEM sheep model used a small number of elements, insufficient to capture steep pressure waves inside the lungs. The same team also has developed an anatomy and image-based multidimensional human thorax FEM model using Visible Man data from NIH/NLM. Tissue-dependent material properties involved an elastic thoracic cage representing the bone, muscle, and cartilage; a low shear modulus incompressible liquid for the abdominal cavity; and a compressible elastic material for the lung. The lung material properties were selected to reproduce the proper compression wave speed. The 3D human thorax/lungs FEM model and the LS-DYNA FEM software tools were used to study biomechanics of thorax and lung responses to blast wave loadings. The model had sufficient resolution to simulate the dynamics of complex pressure waves within the lung and against the heart (Stuhmiller 1997; Stuhmiller et al. 1999). The model simulation results for an open air blast wave showed large pressure gradients on the exposed thorax side at the tips of the diaphragmatic lobes, similar to the lung injury location observed in experiments.

High-fidelity simulation of blast wave loading of a thoracic cavity can be analyzed properly with fully coupled external gas dynamics and body biomechanics. All previously described blast wave lung injury models ignored the gas dynamics coupling by assuming an idealized thoracic pressure loading profile. Furthermore, existing FEM software tools do not provide the capability to simulate the fluid-structures interaction (FSI) problems needed to model blast wave lung injury. In a recent study, CFDRC has developed a fully coupled CFD-FEM FSI model capable of simulating blast wave interaction with a thorax, pressure wave penetration into the tissue, and propagation in the lung (Przekwas et al. 2004; Friend 2005). Visible Human data was used to develop a 2D geometrical model of a thoracic cavity with tissue specific material volume conditions as described previously in this chapter. To simulate blast wave propagation in air, impact on the human thorax, and reflection/diffraction on the body,

the computational mesh extends into the air surrounding the thorax, a necessary requirement for solving this FSI problem. In these simulations the lung parenchyma was assumed to be a viscous, compressible porous air media and solved using the finite volume method (FVM). The rest of the tissue (muscles, rib cage) was treated as a solid and modeled with FEM. It was assumed that the lung behaves as a two-phase (air and tissue) porous media with compressibility, $d\rho/dp$, adjusted to match the lung sound speed c (i.e., $d\rho/dp = 1/c^2$). Table 7-2 presets the material properties used in their simulations.

At a distance from the thorax an inlet boundary condition was specified with the plane wave pressure wave taken as a Gaussian pulse:

$$P = \exp\left[\frac{-(t-3\tau_p)^2}{(\tau_p)^2}\right] \tag{7.39}$$

where t is time and τ_p is the characteristic time. Figure 7-27 shows sample simulation results for selected time instances during the blast wave engulfment of the human body. Note in Figure 7-27 that the pressure wave propagates from the top (or the front of the body) to the bottom. The results show velocity vector fields in air, deformation in the thoracic tissue, and the pressure map in lungs. Note that the velocity vectors clearly demarcate the propagating shock wave front from the quiescent air in front of the shock. Once the pressure wave front reaches the thorax wall, it compresses the wall (moves the wall downward) and sends a pressure wave into the lung, as shown in Figure 7-27 (t1). Since the speed of sound inside the lung (40 m/sec) is slower than that in the air (340 m/sec), the induced wave front inside the lung is falling behind the blast wave front (see times t1, t2). It can be seen from Figure 7-27 (t2) that the incoming wave is reflected off the thorax body once it reaches an interface with a

Table 7-2 Material Properties Used for Modeling Blast Wave Lung Injury (Przekwas et al. 2004)

Properties	Bone	Muscle	Lung
Young' Modulus, E (Gpa)	11.00	0.675	0.713×10^{-3}
Density (kg/m^3)	2,000	1,000	60
Speed of Sound (m/s)	2,721	1,600	40

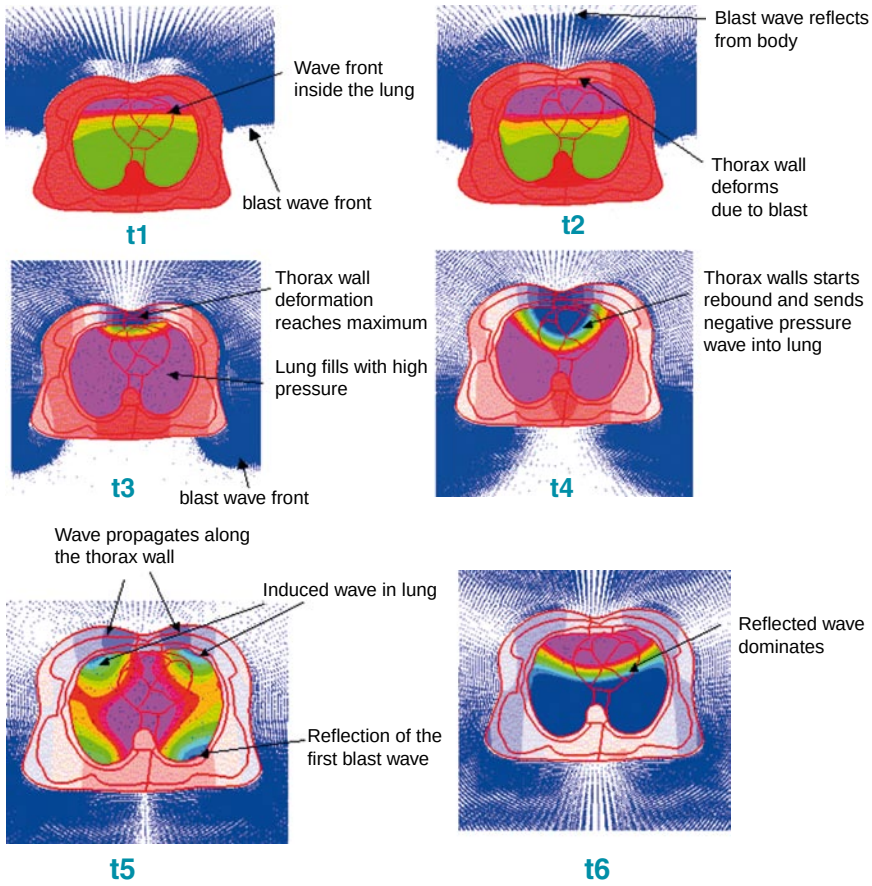


FIGURE 7-27 *Fluid-Structures Interaction (FSI) simulation of blast wave impact on the human thorax; 2D transient simulation results—velocity field in the air, deformation in the thoracic cavity, and pressure field inside lungs (Przekwas et al. 2004).*

different density, and the thorax deforms into the body due to blast wave pressure loading. At time t3 (see Figure 7-27), while the whole lung is filled with high pressure and the shock wave front passes over the body, the thorax sternum wall deformation reaches the maximum and starts to rebound. This thoracic sternum wall rebound actually sends a low-pressure decompression wave back into the lung (see Figure 7-27, t4). At that time the original blast wave front already has passed over the body and two inwardly diffracted pressure waves close at the back (posterior) side of the body. The wave propagation becomes more complex as the pressure wave also propagates along the posterior thorax wall and sends a

different pressure pulse into the lung. At t5 the progressive wave reaches the other end of the wall, and experiences a reflection. This reflection then dominates in the lung (see Figure 7-27, t6).

The computational results presented earlier include detailed pressure, velocity, stress, and strain fields at any instant and any location of the thorax and lungs and provide an indirect measure of the potential lung injury. It is of great interest to develop a quantitative measure of the spatially resolved property that could be used to measure the lung injury potential, similar to Stuhmiller et al.'s (1996, 1998) averaged energy density injury measure. He discovered that the incidence of injury and lethality follow a log-normal correlation with the computed total energy in these waves and when the energy is normalized by the lung volume, the lethality correlation applies to all large animal species. He observed that the correlation could be made between energy density of the waves and observed injury. Przekwas et al. (2004) have proposed a similar injury measure by computing the 3D field of energy density in the lung during the entire blast impact event. The uniqueness of this approach compared to Stuhmiller et al.'s (1996, 1998) INJURY model is as follows.

1. The INJURY model of Stuhmiller et al. (1996) is a compact "point model." It computes an averaged energy density through the whole lung. The present model is multidimensional and provides the spatial distribution of high energy within the lung. This is very critical as regions of large compression and tension were observed in the vicinity of the tip of the lobes, the heart, and the spinal process, and each of these are areas where hemorrhaging is observed (Cooper 1991).

2. The proposed injury criteria model has more detailed representation of the thorax tissue. In a compact model, the geometry of the lung and thorax has been greatly simplified to consider only the area of applied load and the total effective volume of the lung. The details of the internal wave propagation, interaction with internal organs, and viscoelastic forces arising from the thorax itself have been ignored. Without such information, it is not possible to predict the specific location of the injury.

To derive the injury criterion, we start with the energy conservation law: the fluid contained in a control volume (finite element) takes the form of an energy balance, expressing the fact that the sum of the energy fluxes entering the control volume through its boundaries must be equal to the increase of the energy contained in the fluid filling the control volume. This is expressed as:

$$dW + dE_c + dE_M = dE_i \tag{7.40}$$

where dW indicates the energy transferred to the fluid in the control volume as work. The term dE_c indicates energy transported with the fluid, which crosses the boundaries into the control volume by convection. The term dE_M summarizes all other forms of energy transport across the boundaries caused by the molecular movement, for instance by heat conduction. dE_i denotes the increase in the energy stored in the fluid within the control volume. This equation is an expression of the first law of thermodynamics.

Let e be the total internal energy per unit mass, which includes the kinetic energy, then:

$$dE_i = \frac{d(\rho e)}{dt\, dx\, dy\, dz} \tag{7.41}$$

The energy flux transported by the fluid through the surfaces of the control volume is:

$$\rho U_n \, dA$$

with U_n as the normal velocity and dA as the area of the surface. Let the conduction of heat be:

$$q_{i,i} \, dx\, dy\, dz$$

The dW is the work done by the environment on the mass inside the control volume. This work is the scalar product of the force exerted by the environment and the velocity of the particle exerting the force. Since the particle exerting the force on the control volume is itself touching the control volume, its velocity is the fluid velocity at the control volume surface. In tensor form it is:

$$dW = ((u_i p)_{,i} + (u_i \tau_{ij})_{,j})dx\, dy\, dz \tag{7.42}$$

where τ_{ij} is the stress tensor. Now we can write Eq. (7.42) as:

$$\frac{d(\rho e)}{dt} + (\rho u_i e)_{,i} + (u_i p)_{,i} + q_{i,i} = (u_i \tau_{ij}), \tag{7.43}$$

Equation (7.43) is the energy conservation equation in the differential form. If we neglect the viscous dissipation, heat conduction, and convection motion of the fluid, it reduces to:

$$\frac{d(\rho e)}{dt} + (u_i p)_{,i} = 0 \tag{7.44}$$

Integrating this equation across the lung body volume, the total work can be evaluated as derived by Stuhmiller et al. (1996). In this model, the total internal energy for each control volume is evaluated based on Eq. (7.43), from which the energy density can then be obtained. To calculate the normalized work, divide the total internal energy by the local volume and the ambient pressure to get:

$$W^* = (\rho e(t) - (\rho e)_0)/p_0 \tag{7.45}$$

The total internal energy is a function of time and spatial location in the lung. This allows for estimation of the spatial extent of the lung injury. The preceding normalized work model has been implemented into the FSI blast lung injury simulator (Przekwas et al. 2004). The following demonstration simulation presents the results of the earlier energy density blast lung injury model.

The model assumes initial conditions in the air and the lung tissue as atmospheric conditions. A planar shock wave is imposed in front of the thorax and the shock strength is computed based on initial overpressure of $p = 30 \times 1.0^5$ (N/m^2) and $T = 4{,}500$ K. Figure 7-28 shows the sequence of images from the simulation of shock wave propagation into, around, and through the human thorax, similar to the test case presented earlier. Once the pressure wave front reaches the thorax wall, it compresses the wall (moves the wall inward) and sends a pressure wave into the lung. This pressure wave creates a local high energy density as shown in Figure 7-28 ($t = 0.4$ ms). Two wave fronts can clearly be seen: (1) the original energy wave front outside the chest wall, and (2) the internal induced energy wave. What is important is the internal energy wave. All the wave strength has been normalized from 0.0 to 1.0 for clear visualization. Since the speed of sound inside the lung (40 m/sec) is slower than that in the air

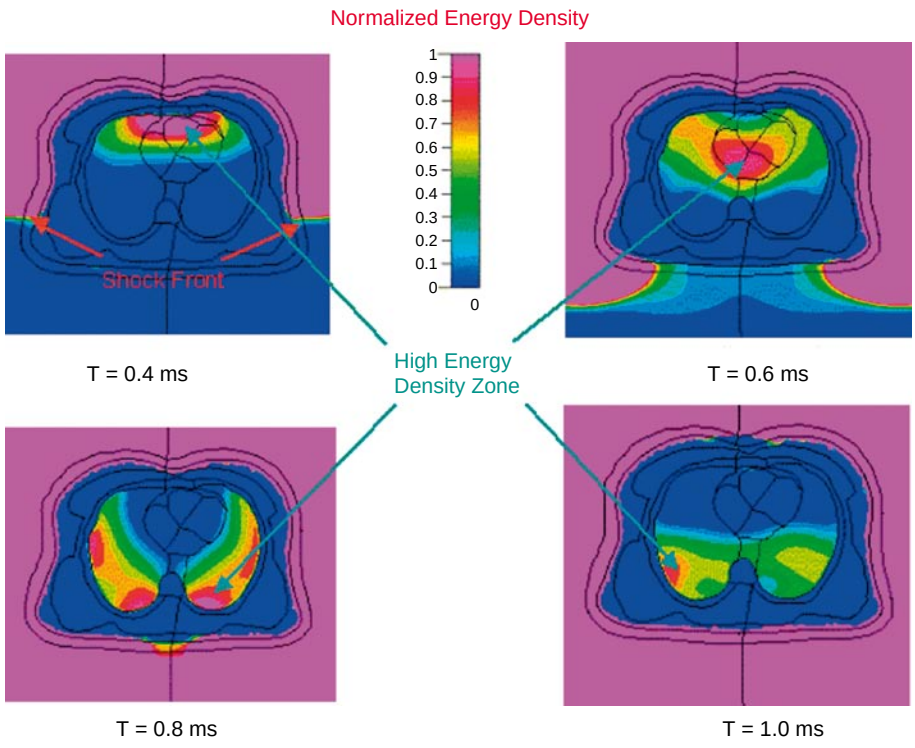


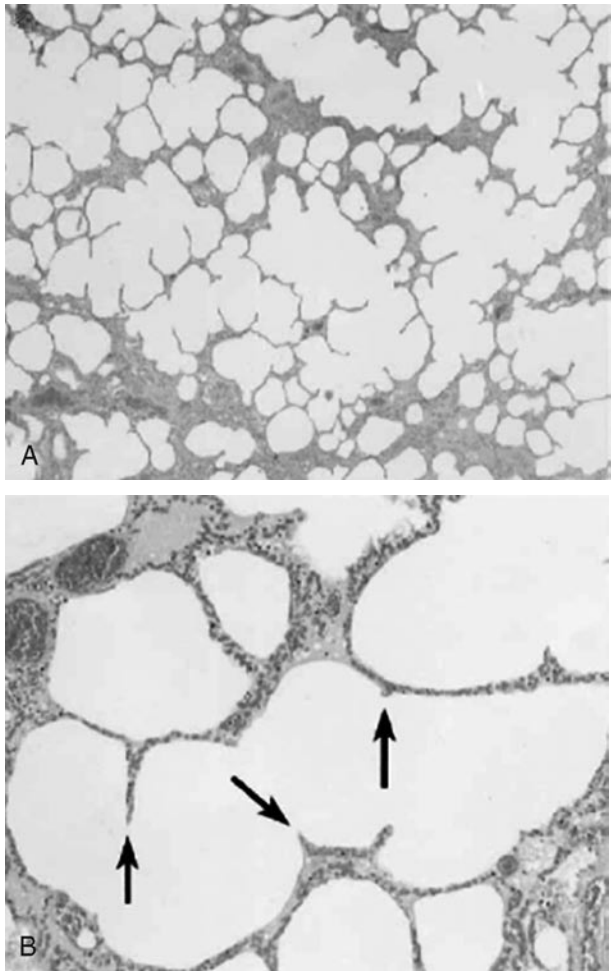
FIGURE 7-28
Normalized energy density field during the blast wave passing through the thorax (Przekwas et al. 2004).

(340 m/sec), one can see the induced wave front inside the lung is falling behind the blast wave front. From Figure 7-28 (t = 0.6 ms), it can be seen that there is a local high energy density zone moving inside the lung. At t = 0.8 ms, the high energy density zone reaches both back sides of the lung and starts to reflect. At t = 1.0 ms, the high energy zone rests in the back of the lung.

High-fidelity fluid-structures interaction simulations of macroscopic lung injury biomechanics provide time dependent pressure wave data for microscopic alveolar scale models. Alveoli scale models should encompass the air space, surfactant, alveolar septa, and pulmonary capillary vessels. The alveolar septum is a very thin structural framework that ensures a minimal barrier between air and blood, while a relatively enormous surface of contact is maintained for efficient gas exchange. It consists of a skeleton of fine elastin and collagen fibers, which are interlaced with a capillary network. It is generally accepted that mechanical stresses within the alveolar septum and on embedded pulmonary capillaries play a critical role in the lung injury

mechanism (Gorbunuv 1997; West 2003). At the microscopic level, the blast induced pressure wave in the lung may cause several mechanical perturbations in the lung tissue and associated vasculature: shear and normal stresses, increase in surface tension, vibrations, potential collapse of the alveolar sacs and displacement of the alveolar surface liquid, tearing off alveolar membranes, and rupturing the blood vessels. Figure 7-29 shows sample microscopic histology images of blast injured alveolar septa with severe alveolar overdistension of alveolar spaces, ruptures, and thinning of alveolar septae (Tsokos et al. 2003).

FIGURE 7-29
Histopathology of human blast lung injury. ***(A)*** *Image of severe alveolar overdistension: enlargement of alveolar spaces, ruptures, and thinning of alveolar septae.* ***(B)*** *Closer view of ruptures (arrows) and thinning of alveolar septae (Tsokos et al. 2003).*



Higher energy stress waves penetrate deep into the lung and produce characteristic multifocal hemorrhages under the pleura where the blast front impacts the chest wall, as well as near the diaphragm and mediastinum, where reflections and summations of stress waves occur. At high overpressure injuries, blood will completely fill alveoli and respiratory/terminal bronchioles (Argyros 1997). During hemorrhage, red blood cells may also rupture and release hemoglobin, which in turn may trigger a cascade of events leading to oxidative stress. Edema, another chronic complication after blast injury, occurs in the first few days after the blast injury and is characterized by extensive epithelial and endothelial barrier damage, resulting in the flooding of alveolar air spaces with proteinaceous liquid, inflammatory cells, and fibrin. Systemic hypoxia further augments fluid filtration, inhibits Na^+ reabsorption, and causes alveolar flooding and thickening of the diffusion barrier for oxygen.

Dynamic oscillations of the septum walls and capillary bed will cause not only alveolar edema and hemorrhage, but also air embolism (air inflow into blood vessels and then to the systemic circulation). It most likely originates from pressure wave

enlargement of the airspace and disruption of alveolar septae and interstitial vessel walls with consecutive air absorption into the adjacent pulmonary veins. Figure 7-30 schematically illustrates blast induced hemorrhage and embolism. Air embolism is considered one of the chief factors leading to cardiac dysfunction and immediate death after blast wave exposure. Air embolism can also be caused by mechanical ventilation of blast victims.

High fidelity mathematical modeling of blunt or blast wave alveolar biomechanics and injury have not been reported to date. Simplified FEM biomechanics model of alveolar structures recently have been demonstrated by Gefen et al. (2001), for a small section of single alveolar wall, and by Denny & Schroter (2006), for an assemblage of 91 idealized alveoli—identical truncated octahedra arranged into a cuboidal block. The geometry of a typical alveolar structure can be generated from a scanning electron micrograph of lung parenchyma tissue. Figure 7-31A presents part of a mouse's fixed lung parenchyma (Lawrence Berkley Laboratories, USA; http://www-itg.lbl.gov). Based on such septal wall morphology, Gefen et al. (1999, 2001) constructed a conceptual biomechanical model of an alveolar wall with embedded capillary (see Figure 7-31B) and used an idealized 2D FEM

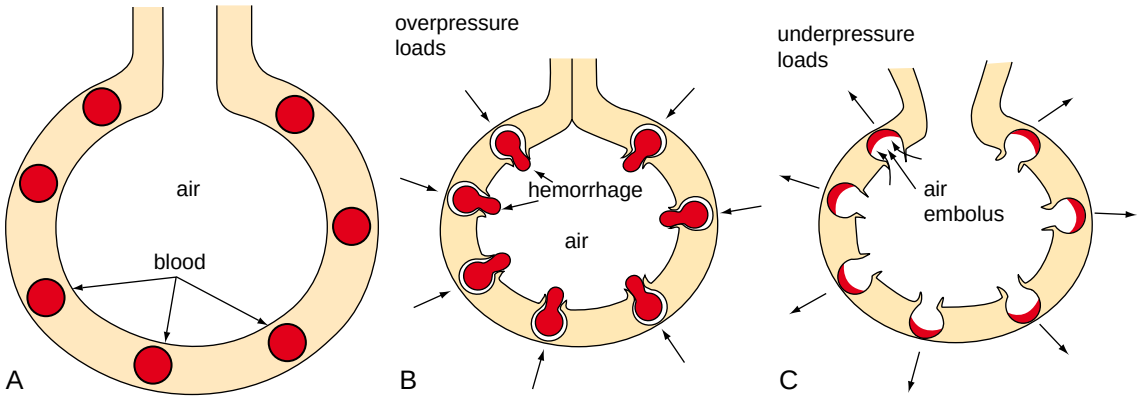


FIGURE 7-30 *Schematic illustration of a dynamic blast pressure injury to lung alveoli.* ***(A)*** *Lung alveolus with blood capillary bed.* ***(B)*** *Overpressure compressive loads cause breakup of capillaries liquid spallation and blood hemorrhage into air space.* ***(C)*** *In the subsequent underpressure phase the air overexpands and is pulled into the capillaries causing micro emboli.*

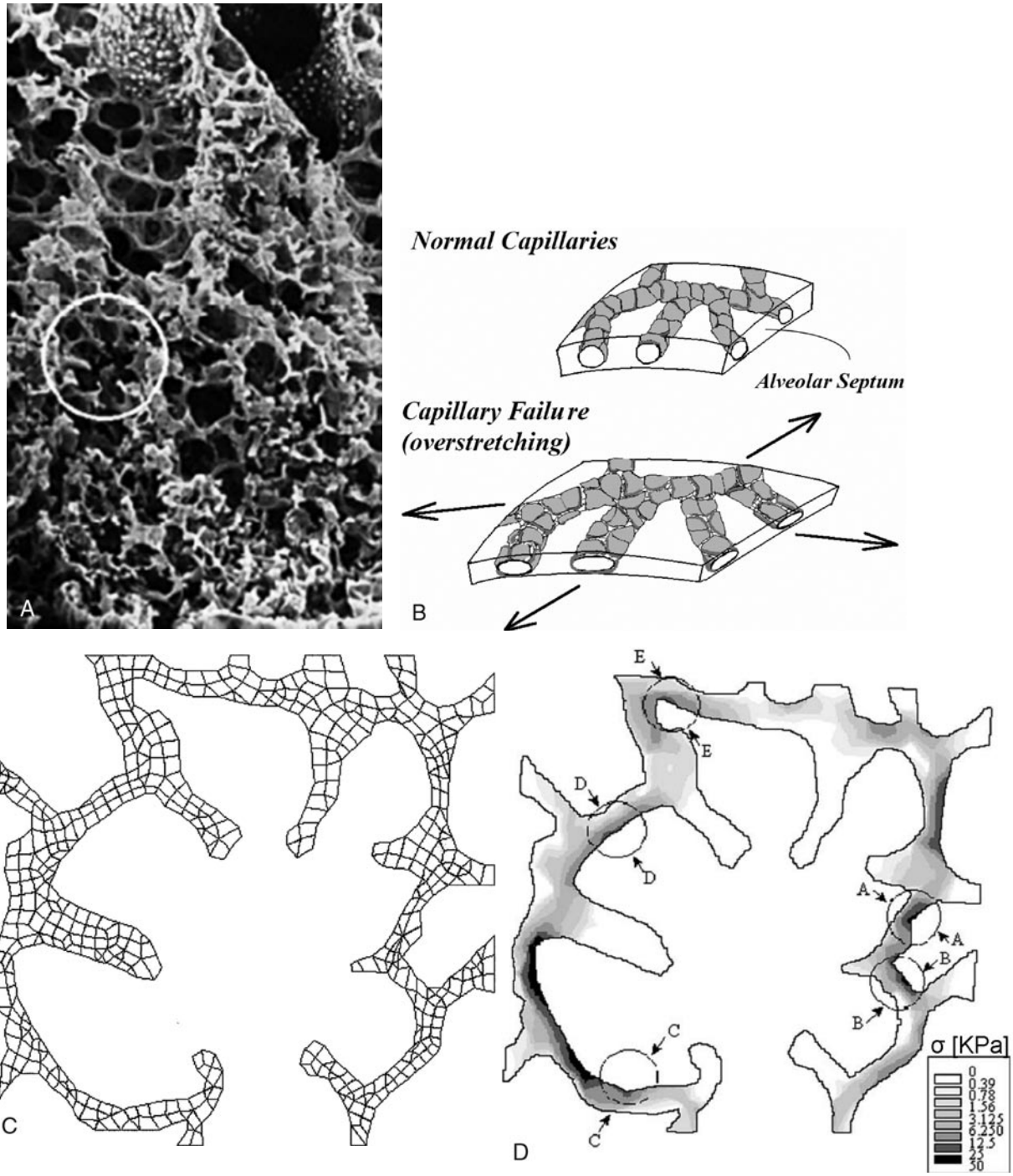


FIGURE 7-31 ***(A)*** *Example of a histological image of an alveolar cluster (Lawrence Berkley Laboratories) and* ***(B–D)*** *Gefen alveolar mechanics model (****B****–concept,* ***C****–2D FEM mesh, and* ***D****–predicted distributions of principal tension stresses Gefen et al. (1999, 2001).*

model of an alveolar structure (see Figure 7-31C) to analyze the mechanical deformations during pressurization of the structure. His model assumed unstressed septal walls at $V_{LO} = 35\%$ of total lung capacity, a uniform prescribed air pressure in all alveoli, and constrained traction at the alveolus "mouth" and cut-off septal walls. Figure 7-31D presents predicted distributions of principal tension stresses for a specified pressurization level p_A. As expected he found increased stress concentrations at locations of small curvatures (circles in Figure 7-31D).

Construction of an alveolar scale FEM model inside the lung parenchyma to study pressure wave dynamics is challenging because of difficulty in specification of boundary conditions. Such a model, however, would be very useful to enhance our understanding of the biomechanics of septal walls during pressure wave propagation. It could be used in conjunction with the thorax scale model to identify regions and extent of primary lung injury. It could also be used to compute initial conditions for modeling an alveoli scale secondary injury events, including reduction of air-blood gas exchange, edema and hematoma formation, immune responses, mechanical ventilation, and others. The next section presents an example gas exchange model in healthy and injured lung.

Models of Lung Gas Exchange and Respiration Injury

The respiratory system is responsible for gas exchange between the air in the lung and the circulating blood. The rib cage and diaphragm muscles draw air into the lungs and then release it back to the atmosphere. The normal human lung is maintained in an inflated state by the negative pressure environment of the thoracic cavity. Gas exchange with the pulmonary circulation begins at approximately generation 17 of the airway tree (the respiratory bronchioles) and extends to the terminal alveolar ducts and alveolar sacs. Computational modeling of the lung respiration process, gas exchange, and pulmonary circulation before and after mechanical injury would enable detailed analysis of secondary lung and systemic injury events, such as alveolar flooding and reduced oxygen exchange with the pulmonary circulation. A combined model of lung physiology, systemic circulation, respiration, and metabolism could be used to study whole body secondary injury events such as hypoxia, embolism, immune responses, and potential treatment planning. This and the next section present example modeling

techniques for lung physiology, injury, and systemic whole body and cardiopulmonary circulation.

Significant research has been done on the modeling of respiration physiology. A survey of the literature reveals several mathematical models of different aspects of the lung respiration system. Some of the models describe the whole system, and others provide detailed insight into the functionality of specific subsystems. Modeled respiratory system functions include the gas flow in and out of the lung, gas exchange between lung and blood, and gas dissociation in blood and the blood transport system. To study the airflow (convection and diffusion) in the respiratory tree, it is natural to apply Computational Fluid Dynamic (CFD) modeling technology. For example, Kunz et al. (2003) have used CFD to simulate particle transport and deposition in the human lung. However, due to the complexity of the lung (i.e., geometry), the huge number of branches, the temporal variation, and the lack of data/parameters, most lung respiration simulations are based on simplified 0-dimensional compartmental models (Benallal et al. 2002; Lu et al. 2002; Brighenti 2003). In compartmental models, the lung typically is represented as one or a few well-mixed reactors coupled to a systemic blood circulation model via the alveolar air-blood gas exchange model (Lu et al. 2002).

In a recently developed multiscale model of lung physiology and blast induced lung injury, Przekwas et al. (2004) and Ding et al. (2005) have combined the 3D air respiratory tree model with submodels of alveolar gas exchange and the pulmonary vascular bed. The model allows simulation of locally induced lung injury, lung hemorrhage, and reduced gas exchange, and can be linked to the pressure wave dynamics in the thorax described earlier and to the systemic whole body circulation, metabolism, ischemia, and other secondary injury mechanisms. Airflow in the lung airway is simulated using transient 3D Navier-Stokes equations with chemical species (O_2, CO_2) mixing. Alveolar gas exchange is simulated using a Macro Air Sac System (MASS) Model (Ding et al. 2005). In this approach, hundreds or thousands of macro computational air sacs are created, with each of them connected to one of the end branches of the computational lung airway (see Figure 7-32). Each individual macro air sac represents thousands of real lung alveoli and its effective properties (surface area, volume, gas diffusion exchange coefficient). Key features of the MASS model can be summarized as follows:

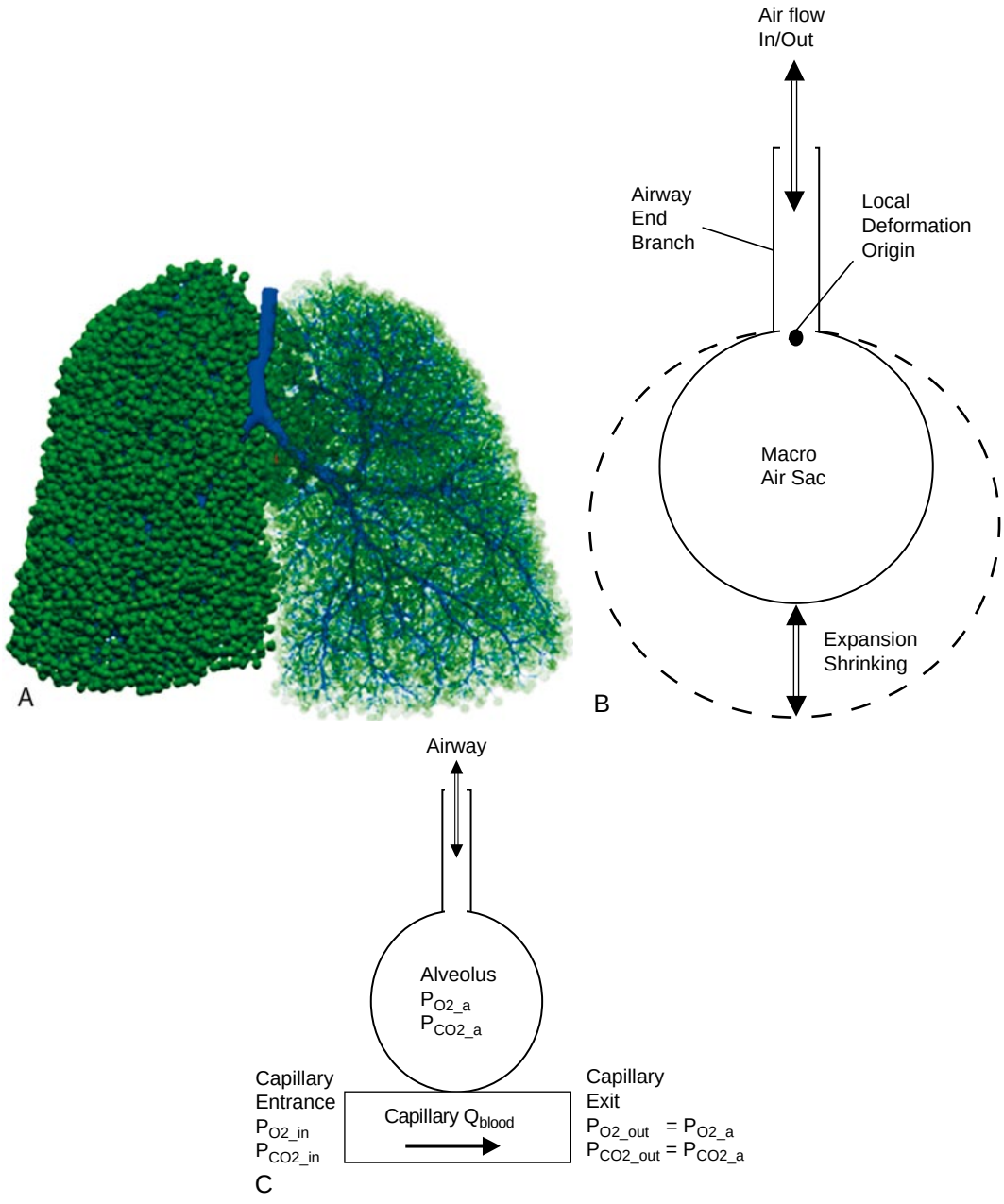


FIGURE 7-32 *A multiscale model of a respitating lung and a Macro Air Sac System (MASS) model used for modeling alveolar gas exchange (Ding et al. 2005).*

- Each macro air sac is represented by a single meshed spherical polyhedron.
- Total volume of all the macro air sacs is kept the same as the total volume of real lung alveoli.
- The volume change of the lung is realized by the grid deformation of the macro air sacs. The total volume change of macro air sacs during transient simulation is set to be the same as the total volume change of the real lung alveoli during the respiration process.
- Due to the huge size differences, the diffusion in macro air sacs will be significantly different from the diffusion within the real tiny alveoli if the same diffusion coefficient is used. Therefore, the gas diffusion coefficients inside the computational macro air sacs must be adjusted to assure the same diffusion effects. Those coefficients can be evaluated using the following formulation:

$$\frac{D_{comp}}{D_{real}} = \left(\frac{N_{real}}{N_{comp}} \right)^{\frac{2}{3}} \tag{7.46}$$

  where D_{comp} is the diffusion coefficient of computational alveoli, D_{real} is the coefficient of real alveoli, N_{comp} is the total number of computational macro air sacs, and N_{real} is the total number of real alveoli.
- The surface area used in the gas exchange model of the macro air sacs will also need to be matched to the total surface area of the real lung alveoli it represents.

The MASS model accounts for the oxygen partial pressure, oxygen binding to hemoglobin, hemoglobin saturation, carbon dioxide dissociation, and the alveoli perfusion by pulmonary capillaries. The lung expansion/contraction dynamics is prescribed based on a predefined motion of the diaphragm. This is probably the first reported model of a respirating lung using a time dependent moving deforming mesh. Compared to simplified 0-D compartment models, this approach can readily take into account various lung asymmetries, nonuniformity of lung parenchyma, and the dynamics of gas exchange in pathological conditions (e.g., after the blast injury).

The lung simulation model described earlier has been used to simulate the physiological respiration of a typical human adult lung at rest.

Features and parameters used in the validation test case are summarized as follows:

- The initial airway structure was generated from medical image data and the remaining branches are populated based on a tree generation mathematical optimization algorithm (Ding et al. 2005).
- Total number of macro air sacs used in simulation is 2,000.
- Total initial volume of macro air sacs is 2.7 L, tidal volume is 0.5 L, and the total dead space is 0.15 L, typical values for the human lung volume at rest.
- The breathing frequency is 12 times/min.
- To achieve a respiration cycle independent solution, a transient simulation run for 10 respiration cycles (that is 50 seconds with time steps set as 0.1 second) was conducted.
- The cardiac output (total blood flow rate) is 6 L/min.
- The capillary in-flow O_2 partial pressure is 40 torr (mmHg), and the CO_2 in-flow partial pressure is 46 torr.
- The fresh air O_2 partial pressure at sea level is 160 torr, and the CO_2 partial pressure is close to zero.

Model details and analysis of simulation results are presented in Ding et al. (2005). Figure 7-33 shows predicted O_2 and CO_2 concentration changes in the airway and macro alveoli during the inhalation stroke of one respiration cycle (note that only half of each image shows concentration, whereas the other half shows the alveoli and branching geometry for clarity). The three images depict the end of exhaust, mid-inhalation, and the end of exhalation time instances for O_2 and CO_2 concentrations. The initial O_2 concentration is very low (blue color) and at the end of inspiration O_2 raises to its maximum level. During the expiration stage (not shown) oxygen is removed by pulmonary capillaries and decreases to its minimum level. As seen in Figure 7-33 the time variation of CO_2 concentration is a reverse situation compared to O_2.

Table 7-3 shows several key integrated simulation results from this simulation compared with values reported in the literature. In the table, the end tidal CO_2 partial pressure is the maximal partial pressure of exhaled CO_2 at the end of expiration. The respiratory quotient is the ratio of the volume of carbon dioxide expired to the volume of oxygen consumed in a given period of time. The widely accepted value for O_2 consumption shown in the table

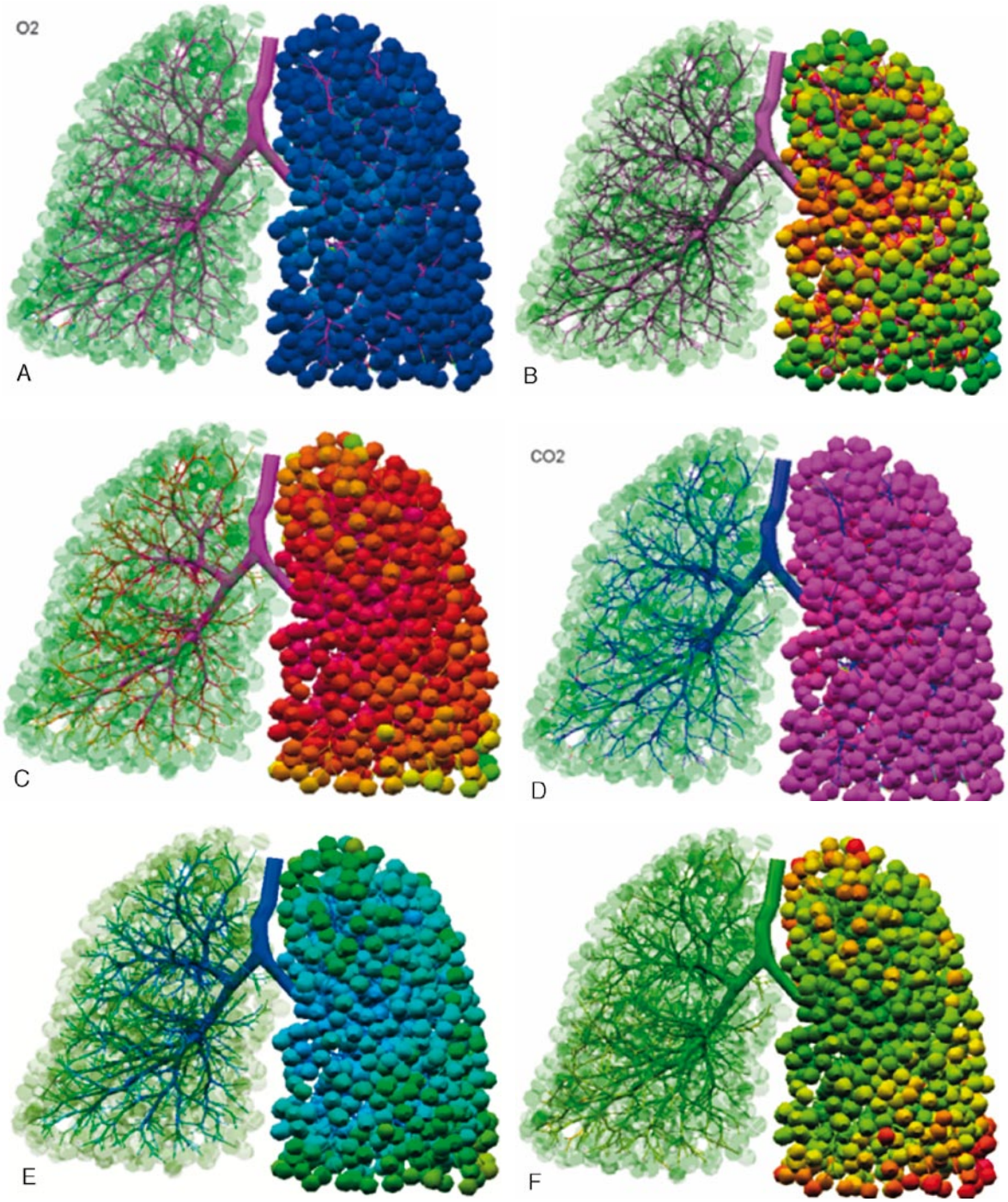


FIGURE 7-33 *Predicted O_2 and CO_2 concentrations in a respirating lung shown at three time instances during inspiration subcycle (Left completely expired, Right fully inspired) (Przekwas et al. 2004, Ding et al. 2005).*

Table 7-3 Comparison of Predicted and Measured Physiological Parameters of a Lung

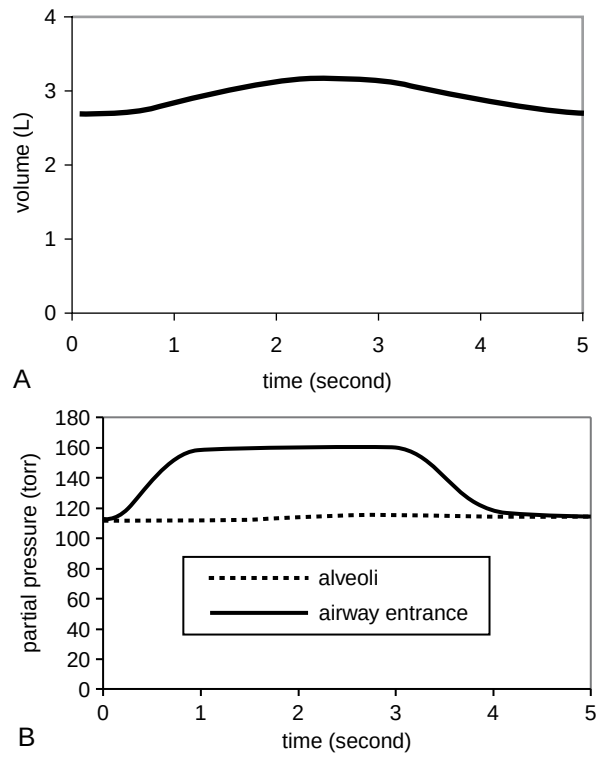
Integrated Value	CFDRC Simulations	Physiological Widely Accepted Values
Average alveoli O_2 partial pressure (torr)	113	100
Average alveoli CO_2 partial pressure (torr)	40	40
End tidal CO_2 partial pressure (torr)	40	40
Respiratory quotient	0.85	0.82
O_2 consumption (M^3/s)	4.8E-6	4E-6

is converted from basal metabolism rate (BMR). The basal metabolism is defined as the rate of energy utilization under minimum stress. For a typical adult, the BMR is around 7000 KJ/day. Assuming a metabolic rate of O_2 as 20 kJ/L, the converted O_2 consumption will be 4E-6 m^3/sec. Note the very good agreement between experimental and computational data.

Figure 7-34 presents the time history of lung volume and oxygen partial pressures at the airway entrance and in the alveolar space during a single respiration cycle for a normal (uninjured) lung. The time variation of total lung volume, which varies from 2.7 L to 3.2 L, is shown in Figure 7-34A. Figure 7-34B shows oxygen partial pressure at the airway entrance (solid line) and the average oxygen partial pressure at the alveoli (dotted line). During the inspiration half cycle, oxygen partial pressure at the airway entrance is the same as fresh air oxygen partial pressure (160 torr). During the expiration half-cycle, the airway entrance oxygen partial pressure is very close to the average oxygen partial pressure at the alveoli. Compared with the situation at airway entrance, variation of averaged alveoli oxygen partial pressure is insignificant during the whole respiration cycle.

FIGURE 7-34

(A) *Total lung volume variation during one respiration cycle and* ***(B)*** *O_2 partial pressures at the airway entrance and in the alveoli in one respiration cycle (Ding et al. 2005).*



In a truly comprehensive human body blast injury model, the preceding lung respiration model should be integrated with the human

body and lung biomechanics models. The lung mechanical injury model can provide the spatial distribution of total energy density absorbed and dissipated by the lung parenchyma. That data, combined with a local model of alveolar injury, can be used as input for 3D modeling of lung respiratory and pulmonary gas exchange pathophysiology. The time scale of the initial shock wave injury is much shorter than the lung trauma response. These models can be executed sequentially, with the mechanical injury model providing input to the lung respiration model. Blast injuries may impair alveolar function by several mechanisms including:

- Reduced capillary blood flow due to capillary leakage and compression (e.g., due to edema)
- Increased air flow resistance or decreased expandability of alveoli due to damage of airway, lung muscle, and/or ribcage
- Increased gas exchange resistance caused by fluid accumulation on alveoli surface due to edema or hemorrhage

In preliminary lung edema injury simulations, Ding et al. (2005) postulated that part of the lower left lung lobe will be partially flooded by edema fluids. The blocked alveoli will therefore not participate in gas exchange. All other parameters in this lung edema injury simulation are set the same as the previous normal lung case shown in Figure 7-34. Figure 7-35 shows plots of the total effective air sacs volume for the injured lung with approximately 35% of total alveoli volume lost due to alveolar edema flooding. The effective tidal volume also reduces proportionally from 0.5 L to 0.32 L. However, the dead space volume does not change that much. The breath efficiency (tidal volume minus dead space) is almost reduced to half. Figure 7-35B shows the O_2 partial pressure in the alveoli and at the airway entrance. Due to the low efficiency of breath, the average O_2 partial pressure in the alveoli is 81 torr, which is much lower than the value of the normal lung. Blockage of the airway also reduces the blood flow participating in gas exchange by the same percentage. Therefore, as we may expect, the total O_2 supply dropped to 2.6E-6 m^3/sec, which is significantly below the amount of oxygen required by the usual basal metabolism rate. To compensate for the shortage of O_2 supply, the human body may respond by increasing the cardiac blood output, increasing breathing rate, increasing the breath depth, or a combination of these. Ding et al. (2005) has performed parametric simulations to analyze the compensatory autoregulation effects on the oxygen delivery to the body. He found that the increase of the cardiac blood output is the most efficient way to

increase the oxygen supply. The increase of breath frequency is less effective due to the low breath efficiency.

A natural extension of the lung respiration model would be to explore models of water balance, accumulation during interstitial or alveolar edema, and lymphatic clearance. There appears to be sufficient experimental and clinical data to formulate, calibrate, and validate such a model. It could be linked to systemic circulation and metabolism models to enable systemic hypoxia and ischemia studies. The model should include both the Starling forces (hydrostatic and protein osmotic pressures) of water transport in the alveolar-interstitium-capillary space but also active ionic transport (e.g., via sodium channels) across the alveolar epithelium during water reabsorption. Ultimately the model could include pharmacokinetics and pharmacodynamics action of pharmacologicals such as catecholamine compounds that influence alveolar fluid clearance, and others that modulate immune responses and control capillary permeability.

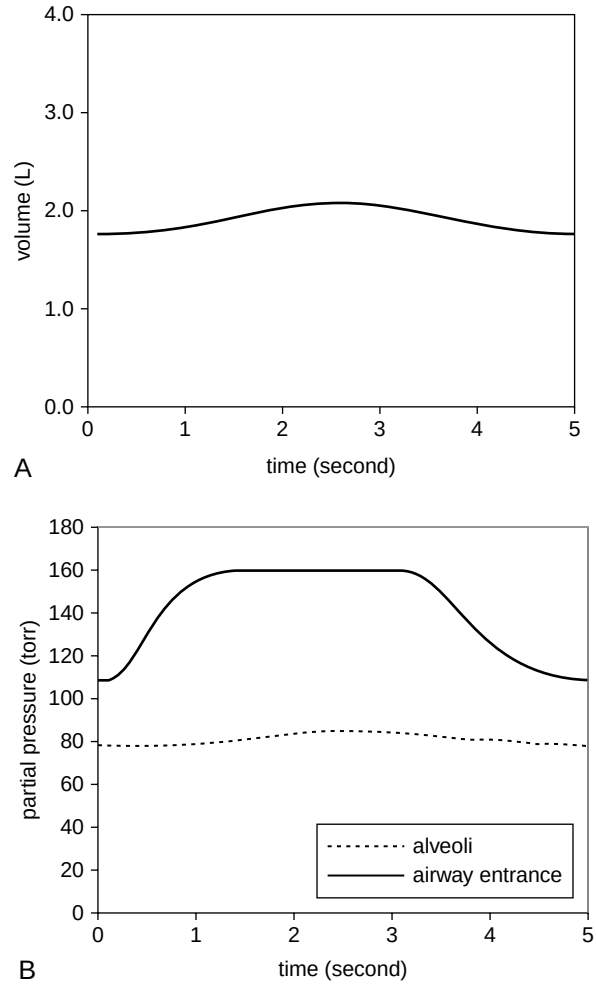


FIGURE 7-35
Performance of an injured lung by edema. ***(A)*** *Total lung volume variation and* ***(B)*** O_2 *partial pressures at the airway entrance and in the alveoli (Ding et al. 2005).*

Whole Body Cardiopulmonary Circulation/Respiration and Injury Models

The physiologic responses following blast injury involve cardio-respiratory, hemodynamic, neural, and immune responses at the systemic, organ, cellular, and molecular scales (Guy et al. 1998; Elsayed & Gorbunov 2003; Wightman & Gladish 2001; DePalma et al. 2005; Gorbunov et al. 2005; Chavko, Prusaczyk & McCarron 2006). At the systemic scale, blast exposure causes an immediate apnea (brief pause in breathing), followed by fast and shallow breathing and oxygen insufficiency. This transient hypoxemia is followed by a gradual recovery to control levels thanks to autoregulation. The heart rate responds with an immediate

bradycardia (reduced heart rate), and drop in the mean arterial blood pressure (hypotension), which is more severe with higher intensity blast waves. Depending on the injury severity, the cardiovascular recovery time to preblast values ranges from hours to several days. Blunt and blast chest trauma is also accompanied by a variety of EKG disturbances that are usually temporary but might account for some fatalities. The timing of the impact relative to the cardiac electromechanical cycle may be of critical importance on sudden cardiac arrest following blast thoracic injury. Several systemic blast injury symptoms occur hours or days after the primary event. For example, respiratory failure occurring 24 to 48 hours after blast exposure is unlikely to be caused solely by the primary blast. The late mortality after lung trauma is related to multiple organ failure, as a consequence of shock or sepsis, linked to systemic inflammation, as a result of infection or tissue injury. Blast trauma is also evident at the cellular and molecular level. Primary events such as edema, hematoma, or hypoxemia, cause oxidative stress in the lung, cytokine "storms," and other immune and host defense mechanisms.

This brief review of the secondary injury events and mechanisms indicates that a comprehensive physiology-based whole body mathematical model coupling circulation, respiration, metabolism, autoregulation, and immune responses could be very valuable in better understanding of blast injury trauma, resuscitation, and pharmacological treatment planning. Such a model has not been established yet, but most of the essential model components already have been developed and demonstrated. Several whole body circulation models have been reported ranging from compartment models (Guyton, Coleman & Granger 1972; Ursino 1998; Lu et al. 2001, 2002; Ottesen, Olufsen & Larsen 2004) to distributed 1D models coupling the arterial network, heart, and lung models (Olufsen et al. 1999, 2000; Ottesen et al. 2004; Taylor & Draney 2004; Sherwin et al. 2003) to quasi 3D multiscale models (Przekwas et al. 2004, 2006). Cardiopulmonary autoregulation models involving baro- and chemoreceptors as well as baroreflex controls of heart rate, myocardial contractility, vasomotor tone, vagal, and sympathetic pathways have been developed (Lu et al. 2001, 2002). Similar autoregulation models exist for chemoreflex and respiration control (Magosso & Ursino 2001). Mathematical models of cell biology and biochemical pathways including immune modulation are emerging at a breathtaking pace (Asthagiri & Lauffenburger 2000;

Tyson, Chen & Novak 2001; Tomita 2001; Sauro et al. 2003). There are also system-level human body mathematical models describing biochemistry and immunology of hemorrhage injury, trauma, and shock states (Chow et al. 2005). Development of a system level whole body secondary blast injury model at various levels of sophistication, from compartmental to distributed, is very feasible. The following presents an example multiscale model of whole body circulation, respiration, and simple metabolism, under development at CFDRC.

With minor exceptions, most of the systemic circulation models use a compartmental modeling approach, assuming the vascular system and individual organs as flow reservoirs and connecting resistors (or resistors, capacitors, and inductors in an electrical analogue) (Ursino 1998; Lu et al. 2002; Ottesen et al. 2004). The limitations of those models are that they cannot simulate the convective transport, vascular elastic wave, and flow and species dispersion phenomena. In the multiscale model briefly presented next, systemic blood vessels can be represented as 1D, 2D, 3D entities or a combination of them. The model maintains 3D geometry of blood circulation in several branching levels of the arterial and venous vascular tree and constitutes a closed complete arteriovenous system. Individual organs and the perfused tissue can be represented either through compartment, distributed, or full 3D models. The model solves fundamental Navier-Stokes equations in all blood vessels using a fully implicit time-domain solution scheme. A fully unstructured mesh is used. The flow equations are coupled to vessel viscoelastic equations with nonlinear wall compliance via the instantaneous pressure at each point along the vessel. The arterial system is pumped by a "heart model" with a parametric equation for time dynamics of ventrical volume variation, that enable heartbeat resolved simulations. Distributed organ and tissue models are used to simulate the connections between the arterial and venous trees. The model was tested against the data and parameters used in the arterial circulation model developed by Olufsen et al. (1999, 2000) and Ottesen et al. (2004). These provided benchmark data for time dependent pressure and flow in the ascending, thoracic, and abdominal aorta, the common and external iliac, and the femoral arteries; all given for one heart pulse period. The circulation model was simplified to an arterial system only, and the capillary beds and venous return were modeled using the Windkessel model (Olufsen et al. 1999, 2000).

The simulation results, shown in Figure 7-36, present time-dependent blood pressure, P, and flow rate, Q, variations at selected arterial locations.

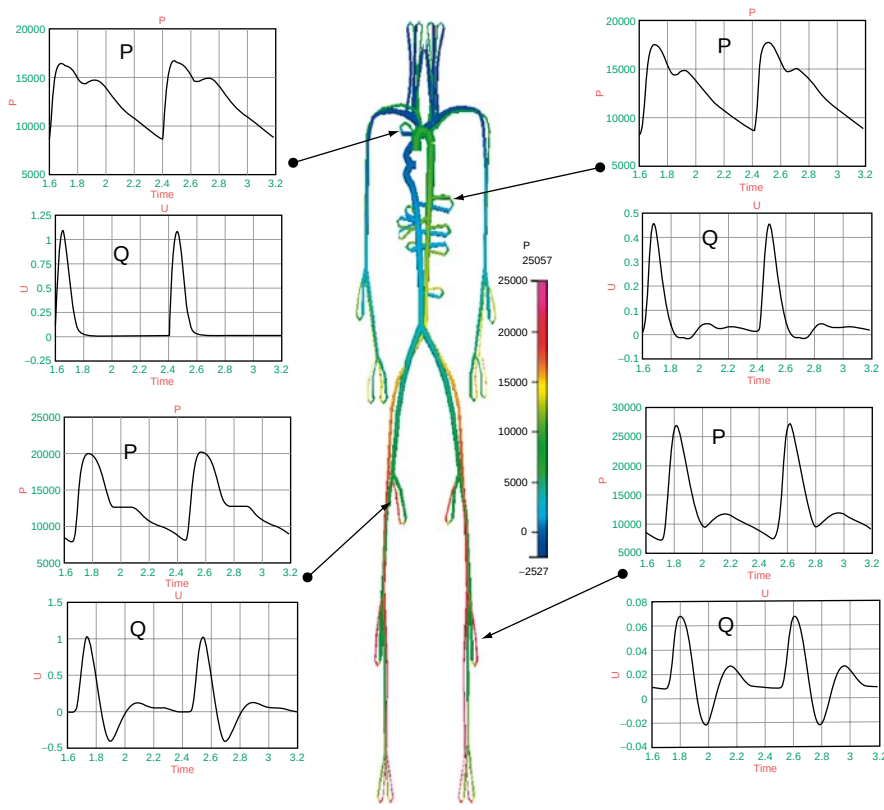


FIGURE 7-36
Arterial flow rate and pressure as function of time at several representative positions in the whole body circulation model (based on the parameter data by Olufsen et al. (1999, 2000).

Very good agreement with the Olufsen model was achieved. It should be noted that because CFDRC used a fully implicit method of solving all vessels simultaneously, versus the semi-implicit method of Olufsen (with explicit method at vessel branches), the CFDRC simulations are an order of magnitude faster and more robust than the Olufsen (1999) model.

The advantage of the multiscale distributed model is that it can be applied to simulate the vascular responses during the primary blast injury events as well as secondary systemic responses. The model uses elastic properties of tissues and vasculature and relates the vascular pressure and tissue pressure. It is possible to apply a blast wave or high velocity impact pressure loading on any part of the body and analyze the cardiovascular compression wave responses in the entire vascular system. When linked to autoregulation, potentially it could be used to study vasospasm events. CFDRC has performed preliminary simulations of a pilot's cardiovascular (arterial and venous) system exposed to high acceleration maneuvers in standing and sitting positions, accounting for gravity and human body accelerations

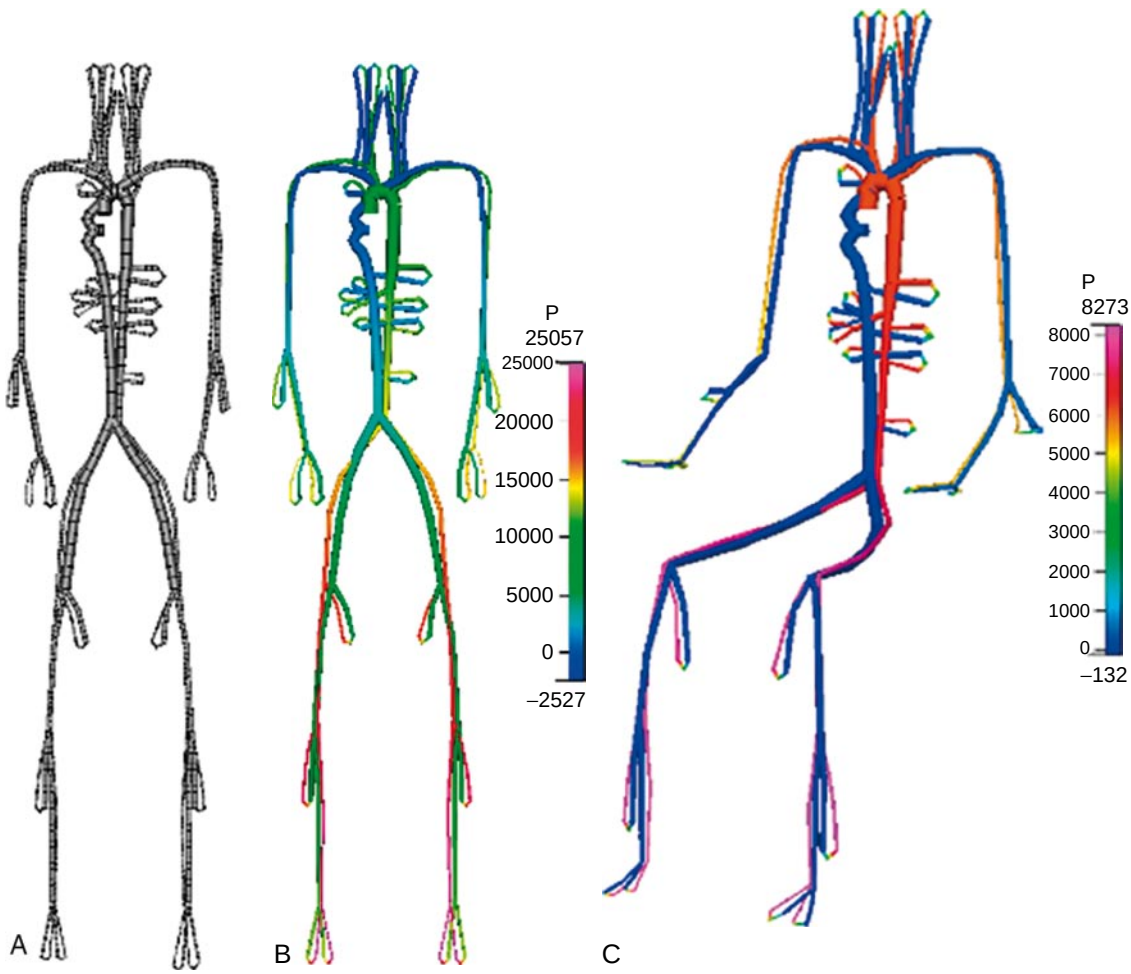
(Wilkerson, Harrand & Przekwas 2006). Figure 7-37 presents whole body vascular mesh and blood pressure profiles at a time instant in a body subjected to sudden acceleration in a standing and seated position.

Modeling of Protective Armor

The development of fiber-reinforced polymer matrix composites, ceramics, and Kevlar late in the last century made the modern generation of bulletproof vests possible. As a result, current personal protection vests with rigid body armor are effective in stopping even high-speed bullets. Although the bullet is stopped, a considerable amount of energy is transmitted through the protective armor and delivered to the human body, often resulting in a blunt injury, a phenomenon known as "behind armor blunt trauma" (BABT). Typical BABT injuries include severe lung and heart

FIGURE 7-37

Three dimensional whole body vascular mesh and blood pressure profiles at a time instant in a body subjected to sudden acceleration in standing and seating position (Wilkerson et al. 2006).



contusions as well as rib fractures (Jolly & Young 2000). The impact energy is transmitted to the body in two distinct mechanisms of energy transfer: (1) first fast wave, generated by initial bullet impact in the form of an elastic stress and deformation wave in the armor that arrives at the body surface with the speed of sound; and (2) distortion wave, generated by the bullet deceleration, plastic deformation of the bullet within the armor, and large spreading elastoplastic deformation wave of the armor material that ultimately arrives at the thorax in the form of a large bulge at the rear side of the armor. The art of armor design is to absorb as much energy as possible in the armor and spread the rear side bulge to the largest possible area (reduce tissue contact pressure). The design of the armor is based on the fact that a reduction in peak pressure will reduce injury, even if the total impulse over the duration of the event is not reduced. A significant amount of experimental and computational research has been expended on the optimization of ballistic armor. Unfortunately, design principles of protective armor against blast injury are much less understood.

Experimental tests of blast waves on pigs have been conducted by Cooper (1991), who analyzed different materials for protecting lung tissue from shock waves. He found that materials composed of a layer of denser material (Kevlar as well as copper and lead) over soft foam can partially protect pigs from blast injury. He concluded that blast protection is more mass, rather than material strength, dependent. Makris & Nerenberg (2000) at Med-Eng Systems Inc. in Canada used a mechanical fixture and instrumented Hybrid II dummies with various demining personal protection ensembles to evaluate their effectiveness against blast injury. A demining ensemble with an energy absorbing composite provided adequate protection against 200 g of C4 explosive. A flak vest, made of layered soft ballistic fabric, did not. In fact it was noticed that bullet protection vests are not very suitable for blast protection. In some cases it was shown that certain vest materials may exacerbate blast lung injury. Several experimental studies of protective equipment against blast explosions recently have been conducted with animals, cadavers, and mechanical surrogates funded by TSWG and other DoD organizations.

Computational modeling of protective equipment against blunt and ballistic impact has been conducted since the early days of FEM technology. Some of the recent examples include the work of Jolly & Young (2000) on 3D FEM models of ballistic impact on armor vest protected human thorax,

Grimal et al. (2004) on quasi 3D models of composite armor-on-tissue FEM models, and on 3D high-fidelity FEM models of the human thorax protected by a ceramic plate (Roberts et al. 2006). High fidelity FEM modeling of composite armor also has been used to study helmet protection of the human head from ballistic impacts. Aare and Kleiven (2007) recently have presented a comprehensive FEM model of the U.S. Personal Armor System Ground Troops' (PASGT) Kevlar helmet with suspension and protective pads placed on a human head. Their model was used to study how helmet shell stiffness affects the load levels on the human head during an impact, and how different impact angles affect the load levels on the human head.

Computational studies of protective armor performance and fundamental structural analyses of composite materials under blast loading are rare. As mentioned previously, the main reason is a lack of robust FSI modeling tools. Most of the blast impact FEM structural mechanics studies assumed pressure loading based on analytical blast wave models, or used input from CFD simulations. Yu et al. (1985) developed a FEM model of a sheep in a protection vest and analyzed its effectiveness against blast wave injury. The analysis showed an increase in pressure and a delay in rise time as the bulk modulus of the vest material was reduced. Review of the latest FEM studies of blast loaded composites shows that most of the models have been applied for simple geometries and boundary conditions, such as clamped plates, and uniform pressure impulses (Xue & Hutchinson 2004; Vaziri & Hutchinson 2006). The main focus of those studies was to advance current understanding of the different responses of multilayer and lattice composites to shock wave loadings, and to study geometric and material nonlinearities during large plastic deformations (Bahei-El-Dinn, Dvorak & Fredricksen 2006). Some of the key effects such as local delamination typically are neglected. Several blast protective composites modeling and design issues remain to be clarified. For example, metallic foams with a cover plate have been used as sacrificial claddings to protect main structures against blast loads. When subjected to a shock wave, the sacrificial cladding undergoes plastic deformation, absorbs energy, and attenuates the blast loads. At the same time it has been reported that in some conditions sacrificial foam claddings may work unexpectedly as a pressure amplifier when the sacrificial cladding is not properly designed (Li & Meng 2002).

To clarify issues of behavior for composite materials under blast loading, CFDRC has conducted one-dimensional computational simulations using

a fully coupled shock wave CFD and FEM model. The simulations assessed the relative effectiveness of different laminations for blast overpressure protection in the chest and lungs (Przekwas et al. 2004). The range of tested materials included variations of soft material layers (modeled as air layers), rigid layers, and blast attenuating foam (viscoelastic layers). The effectiveness of these different protection layers and their various combinations were evaluated based on pressure measurements on the chest wall. The simulations were constructed to study the effectiveness of various composite structures in energy absorption, dispersion, and attenuation of blast waves in comparison to an unprotected thorax. The analysis included (1) lattice of rigid layers separated by air layers, (2) soft elastic pad, (3) lattice of light rigid-soft elastic layers, and (4) a composite with an enhanced outer layer and attenuating foam. It was found that the lattice of rigid plates separated by air pockets resulted in thoracic pressure higher than the incoming blast wave pressure. Computational results of a soft elastic protective pad showed that it can reduce the incoming blast wave overpressure, but the chest will experience multiple pressure waves due to reflection-transmission of the wave through the soft protection pad. Analysis of the lattice of light rigid-soft elastic layers showed that when the blast wave interacts with a series of hard and soft/lower density materials, which have different acoustic impedances, the blast wave cannot effectively transmit across the interfaces for the range of blast intensities. This results in the blast wave front becoming dispersed and attenuated before reaching the chest wall, as a large portion of the blast energy is reflected rather than being allowed to transmit. Finally, it was found that the optimum protection versus weight composite structure involved a combination of a rigid outer layer and a light rigid-viscoelastic lattice inside the armor. CFDRC's results showed that such a composite provides lower peak overpressure and wave dispersion, with a cost of longer duration of the pressure pulse on the thoracic wall.

SUMMARY AND CONCLUSIONS

The goal of this chapter was to introduce the reader to the exciting emerging discipline of computational medicine and biology, from the viewpoint of blast injury to the lung. Mathematical modeling of tissue biomechanics has been evolving for the last few decades, first as a theoretical idea and then, after introduction of the Finite Element Method

(FEM) in the late 1960s and early 1970s, as a computational biomechanics discipline. Most visible applications of FEM-based human body biomechanics modeling are in the automotive crash safety area, where commercial software exists and high fidelity anatomical virtual human body models have been established. Biomechanics models have also been used for military medicine applications, primarily to analyze ballistic impact, behind armor injury, pilot body biodynamics during emergency ejection from the cockpit, and others. Mathematical modeling of blast injury, and lung injury in particular, has been much less prominent, partly because of the physiological complexity and partly due to computational difficulties. Until the early 1990s, blast lung injury was simulated using compact models involving spring, damper, and mass models. FEM-based lung injury models have been investigated since the early 1990s thanks to projects sponsored by the U.S. Army MRMC.

In the last few years, particularly during Operation Iraqi Freedom, there is a renewed interest in blast injury to the lung, and even more so to the brain. Unfortunately, the existing FEM biomechanics software, anatomical human body models, and tissue material properties are not fully developed and need validation. Advanced computational modeling of blast injury is much more than just biomechanics. Computational modeling of blast injury and the resulting trauma is extremely difficult, as it involves a range of disciplines (gas dynamics, structures dynamics, biomechanics, physiology, pathology, biology, biochemistry), time scales (microseconds to days), and space scales (microns size alveoli to meters scale human body and distance from the blast). Better understanding of primary injury events and secondary injury mechanisms will be possible only if truly multidisciplinary models are established, integrating blast explosion physics, anatomical- and image-based human body geometrical models, human body biodynamics, tissue biomechanics, and several physiological models. This chapter provides the overall perspective on the comprehensive multiscale, multidisciplinary modeling of the blast wave injury to a human body, and with emphasis on the human lung injury. It was designed to provide a good balance between mathematical, medical, and engineering disciplines. For each discipline the reader can find not only relevant technical description but also reviews of early pioneering works with citations and reviews of the latest state-of-the-art work.

Creative mathematical modeling in engineering disciplines strikes a balance between simplified mathematical models, often in the form of analytical solutions or 1D formulations, and high fidelity multidimensional models requiring advance numerical methods and high performance computing. The same is true for computational medicine and biology. This chapter was designed to provide descriptions for both types of models with minimum complexity of mathematical equations and maximum explanation of equations. For nonexperts, it is difficult to find details of classical gas dynamics models of blast wave physics, which had their heyday in the 1950s. For quick reference, the reader can find a succinct description of blast wave physics, equations, and relevant references. Of the two key computational disciplines, CFD and FEM biomechanics, the latter is covered in much more detail, because of its direct importance in modeling human body biodynamics, biomechanics, and injury. It was pointed out that the existing FEM models can handle inertial or ballistic human body biomechanics and injury, but not the blast injury. Blast injury modeling requires fully coupled fluid structure interaction (FSI) computational methods and software, which only recently have begun to emerge. The last section of this chapter provides not only biomechanics of blast wave interaction with the human body and primary lung injury mechanisms, but also descriptions of mathematical models of human physiology and pathophysiology of secondary injury events. Mathematical models of whole body cardiopulmonary circulation, respiration, and oxygen metabolism are essential to study systemic responses to blast wave trauma.

A short discussion of personal protective armor against ballistic and blast injuries is presented in the last section. The last section also presents selected illustrative computational examples of multilayer composites subjected to blast loads and their effectiveness against blast injury protection. The reader can find not only a basic description but also several illustrative examples and references to the latest relevant literature. There is no doubt that the rapidly expanding computational medicine and biology discipline will play a major role in improving our understanding in injury pathophysiology, scaling animal experimental data to humans, and in optimization of pharmaceutical and interventional treatments and procedures. Several authorities in academic and military medicine suggest that integrated injury biomechanics and injury pathophysiology models for both animal and humans are urgently needed and hold great potential in saving lives of people and minimizing animal sacrifices.

DISCLAIMER

The views, opinions, and/or findings contained herein are those of the author and should not be construed as an official position, policy, or decision of the Department of the United States Army.

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CHAPTER 8

Biochemical Mechanism(s) of Primary Blast Injury: The Role of Free Radicals and Oxidative Stress

Nabil M. Elsayed and
Nikolai V. Gorbunov

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INTRODUCTION

Explosion is defined as *an event characterized by violent and sudden release of mechanical, chemical, or nuclear energy with the generation of high temperature and gases accompanied by a loud sound and blast shock waves*. Exposure of humans or animals to blast shock waves (BSW) was found to cause complex multiorgan/multisystem injuries, called *polytrauma*. Traditionally, explosives use was limited to military and occupational applications. Thus, they were used militarily in combat and training, and occupationally in certain industrial applications such as breaking rocks to make way for houses, buildings, roads, and bridges, or mining for extracting minerals, metals, and fuels from the ground. Therefore, blast injuries were limited in number and population at risk. However, in recent years the challenges to physicians, researchers, and engineers increased at a very fast rate as military injuries climbed with increasing numbers of wars and conflicts. Blast injury of noncombatant civilians also increased markedly as they now often fall either to unintentional military fire (collateral casualties) (Summerfield 1997; Suljević & Surković 2002) or to indiscriminate terrorist attacks far away from the battlefield in many cities around the world (Asai & Arnold 2003; Rodoplu et al. 2003; Teague 2004; Aschkenasy-Steuer et al. 2005; de Ceballos et al. 2005; Feeney et al. 2005; Lockey et al. 2005; Karp et al. 2007).

The characteristics of explosives have also changed significantly in recent years. On one hand, the magnitude of BSW produced by nonnuclear explosives such as high-impulse thermobaric weapons (HIT) and fuel-air explosives (FAE) have increased considerably. On the other hand, a new pattern of warfare has emerged in which military personnel fighting to secure cities with large populations frequently are exposed to detonation of atypical, nonmilitary-type explosives. They include roadside improvised explosive devices (IEDs). These IEDs are becoming increasingly more sophisticated and powerful, producing more death and injury. In addition, it was reported in the news recently that cars and trucks carrying toxic chemicals such as chlorine gas (Partlow 2007; Bowen 2007) or nitric acid (Bowen 2007; Multinational Force 2007), combined with explosives, have been used or found in Iraq, and propane gas (BBC News 2007) was used in the recent Glasgow airport car bomb attack (BBC News 2007). To meet these challenges, new treatment modalities and more efficient triage methods for mass casualties and faster evacuation and medical treatment

regimens continue to be developed in parallel with research aiming to understand the mechanism of injury and develop effective personal protective body armor and blast-resistant vehicles. Although typical medical treatment usually proceeds in a sequential fashion based on primary symptoms, understanding of the underlying mechanism(s) of blast injury that often have no external signs can help provide emergency personnel with better injury assessment and more efficient treatment modalities (Belanger et al. 2005).

In general, explosives fall into three major categories: mechanical, chemical, and nuclear. Chemical explosives are the category most commonly used in conventional explosions. These explosives are further classified as low-order explosives (LE) that burn or deflagrate rapidly at rates of up to 400 m/sec (312 ft/sec), and high-order explosives (HE), which undergo detonations at rates greater than the speed of sound, 1,000 to 9,000 m/sec (3,281–29,528 ft/sec). Unlike LE explosives, detonation of HE explosives result in very rapid release of large amounts of energy in the form of heat, and pressure from the expanding gases displacing large volumes of air and producing sonic booms as well as BSW.

The destructive ability of the BSW depends upon (1) amplitude of the blast overpressure, (2) frequency of the sound produced, and (3) the kinetic energy of the striking shock wave (Benzinger 1950; Cooper & Taylor 1989; Guy et al. 1998; Gorbunov et al. 2005; Elsayed & Gorbunov 2007). When a BSW strikes the body, it delivers its energy to the tissues and produces mechanical damage to individual cells and tissue barriers affecting many organ and system functions (Benzinger 1950). Consequently, the injured cells release bioactive compounds (cytokines), which send signals capable of altering the immunochemical homeostasis at both the local and systemic levels and thus produce what is known as "blast injury" (Gorbunov et al. 2004, 2005; Elsayed & Gorbunov 2007). The degree of damage from BSW exposure is complicated by many factors such as magnitude and duration of peak overpressure, the medium in which the explosion takes place (open-air, confined spaces, or underwater), and the distance from the explosion epicenter (Phillips & Richmond 1991; Stuhmiller et al. 1991).

Explosion-induced blast injuries have been classified as (Phillips & Richmond 1991; Richmond et al. 1961a; Elsayed 1997a; Harrocks & Brett 2000; DePalma et al. 2005):

- *Primary*, resulting from interaction of the BSW waves with the body
- *Secondary*, resulting from fragments and projectiles energized by the explosion, accompanied by penetrating or nonpenetrating wounds
- *Tertiary*, resulting from body displacement by the blast wind against a solid surface or by collapsing structures (crushing injuries)
- *Quaternary*, including miscellaneous causes secondary to the explosion; for example, burns, smoke or toxic gas inhalation, asphyxia, etc.

Physically, an incident BSW traveling through the tissues results in its deformation and leads to cavitation, inertial resistance, and cleaving, depending on the tissue type (soft or hard). For instance, soft tissues connect, support, or surround other structures and organs of the body (muscles, tendons, fibrous tissues, fat, blood vessels, nerves, and synovial tissues). On the other hand, osseous or hard tissues (bones and cartilages) support soft tissues and protect vital organs. Each type has varying acoustical rigidity or firmness manifested by phasic shift, wave reflection, and wave absorption or interference as shown in Table 8-1. As a result, each tissue will have different responses to an incident BSW and consequently will sustain different degrees of injury (Grau et al. 1998).

Table 8-1 Physical Characteristics of Human Biological Tissues[1]

	Biological Tissues		
Parameter	**Soft (Wet tissues)**	**Hard (Bones)**	**Units**
Density	1–1.2	1.93–1.98	(grams/cm^3)
Displacement elasticity	2.5×10^4	7.1×10^{10}	(dynes/cm^2)
Resistance to tearing	5×10^6–5×10^7	9.75×10^8	(dynes/cm^2)
Tearing index[2]	0.2–0.7	0.05	(cm)
Acoustic impedance	1.7×10^5	6×10^5	(dynes/cm^3)
Speed of sound	1.5×10^5–1.6×10^5	3.36×10^5	(cm/sec)

[1]*Adapted from Graut et al. 1998.*
[2]*Extent of tissue tearing.*

Primary blast injury to the lung from BSW exposure is considered one of the major, more serious, and often fatal, outcomes of PBI (Phillip & Richmond 1991; Elsayed 1997a; Desaga 1950). For a number of years we undertook the task of studying the effects of BSW exposure at Walter Reed Army Institute of Research. This report presents the results of studies conducted in the last 10 years, assesses our present knowledge of biochemistry of blast injury, and proposes new areas for future research.

In the early 1990s at the start of this phase of the blast program, a large volume of research on the biological and physical aspects of blast already had accumulated following studies conducted in Army laboratories in Albuquerque, New Mexico, Silver Spring, Maryland, Washington, DC, among others in the United States as well as other military research centers around the world. In 1992, a study by Liu in China (Liu 1992), reported that significant increase in malondialdehyde (MDA) was observed in the coclear tissue of guinea pigs exposed to explosive charges detonated in open-field. Following up on these observations, we found in a preliminary study of blood drawn from sheep exposed to simulated BSW that blast exposure resulted in increased plasma lipid peroxidation (Elsayed et al. 1993). These observations were later confirmed in a comprehensive study conducted in collaboration with Dr. Valerian Kagan at the University of Pittsburg to assess BSW-induced free radical formation and whether or not oxidative stress does occur (Liu 1992). In that study, we demonstrated, for the first time, that BSW exposure was associated with free radical-mediated oxidative stress and that it involves depletion of endogenous water- and lipid-soluble antioxidants (ascorbate, glutathione, and α-tocopherol), generation of peroxidation products (MDA and conjugated dienes), as well as alteration of Ca^{2+} transport affecting membrane permeability. The results also suggested that Ca^{2+}-mediated oxidative damage to membranes, particularly of erythrocytes, leads to hemoglobin release, formation of ferrylhemoglobin, antioxidant depletion, and widening of the circle of oxidative damage. These findings were further substantiated in another study when BSW was found to induce increases in plasma lipid peroxidation across several animal species including rats, rabbits, and sheep (Elsayed et al. 1997a). These observations led us to suggest that free radical production may be a common biological response to blast exposure, independent of the animal model used, and that oxidative stress may be playing an important role in the initiation of blast injury and its recovery. This was particularly important since hyperbaric oxygen therapy

was shown to improve survival of animals exposed to blast (Damon & Jones 1971), and is the method of choice for clinical treatment from blast-induced arterial and cerebral gas embolism (Mellor 1988; Phillips & Zajtchuk 1991; Argyros 1997). However, hyperbaric oxygen therapy has been shown to increases free radical formation in the blood and to cause lung and DNA damage (Narkowicz et al. 1993; Shinomiya et al. 1998; Demchenko et al. 2000; Ganguly et al. 2002; Speit et al. 2002).

In subsequent studies, we expanded the scope of the investigation and examined the biochemical and pathological responses to BSW in an attempt to elucidate the underlying mechanism(s) of the blast-induced injury. In these studies we tested the effects of varying the magnitude of peak blast overpressure, compared the lung response to single versus multiple exposures, and examined the effect of time after exposure on the extent of lung trauma (Elsayed & Gorbunov 2007; Gorbunov et al. 1997; Mayorga 1997). We have also examined the effects of blast exposure on food intake and exercise performance (Bauman et al. 1997). Beside small animals, we also have examined the cardiopulmonary response of large animals (sheep) to blast exposure (Dodd et al. 1997; Mundie et al. 2000). Since it was believed that the eye, despite being a hollow organ, can resist abrupt pressure changes, we have examined the effects of blast exposure on the ocular system (Petras et al. 1997).

Thereafter, the potential prophylactic effect of preloading the animals with pharmacological doses of different biological antioxidants prior to blast exposure was assessed (Armstrong et al. 1998; Elsayed et al. 2000).

Based on the combined results obtained from these studies, we suggested that blast-induced free radical formation causes lipid peroxidation and antioxidant depletion (Elsayed 1997a, 1997b), which alters the redox equilibrium and leads to oxidative stress, which in turn plays a pivotal role in initiation and propagation of the injury, and in the delayed systemic tissue and cellular damage (Gorbunov et al. 1997; Elsayed et al. 1997b; Elsayed & Gorbunov 2003). In that mechanism, blast-induced hemorrhage would catalyze free radical formation initiating iron-mediated reactions uninhibitable by desfroxamine (Elsayed et al. 1996; Gorbunov et al. 1997; Elsayed et al. 1997b). In subsequent studies, we employed more sensitive biomarkers of inflammation and oxidative stress to refine the proposed mechanism, and suggested that BSW exposure forces redox

cycling of catalytically-active iron, up-regulates the production of pro-oxidants, affects redox status of injured lung, and thus activates redox-sensitive metabolic pathways that play a pivotal role in initiation and propagation of immediate and delayed systemic effects (Gorbunov et al. 2004, 2005, 2006, 2007).

Based on clinical observation of blast victims, and from experimental animal studies, it has been proposed that the biological effects of blast exposure can be defined as *polytrauma* of the auditory, cardiopulmonary, circulatory, gastrointestinal, and nervous systems further complicated by systemic failure. A common feature of this complex clinical picture in the lung is microvascular hemorrhage followed by pulmonary edema associated with acute respiratory distress syndrome (ARDS)-like symptoms and potential acute lung inflammation (Guy et al. 1998; Elsayed & Gorbunov 2007; Gorbunov et al. 2004). The extravasated blood resulting from the compression/decompression cycle associated with the changes in atmospheric pressure following explosive detonation can initiate a cascade of reactions that involve expression and release of various vasoactive and pro-inflammatory paracrine and autocrine factors including reactive oxygen and nitrogen species and catalytically active iron (Gorbunov et al. 2003, 2005, 2006). Indeed, it has been demonstrated recently that there is an association between BSW-exposure and hemorrhage, oxidative stress, reactive oxygen species, release of catalytically-active iron, and pulmonary inflammation. These events were shown to cause remodeling in the lung microvasculature occurring in a redox-dependent manner and under control of redox-sensitive elements, namely thioredoxin (TRX), redox factor 1 (Ref-1), nuclear factor, erythroid-derived 2, like 2 (Nrf2), nuclear factor kB (NFkB), and mitogen-activated protein kinases (MAPK) (Gorbunov et al. 2007; Moran et al. 2001; Ziegler et al. 2001; Watson et al. 2003, 2004). The redox switches driving these effectors depend on an interplay between intra- and extracellular thiol/disulfide and other reduced/oxidized couples (e.g., glutathione/glutathione disulfide, thioredoxin/oxidized thioredoxin, cysteine/cystine, and ascorbate/dehydroascorbate) with cycling electron acceptors in the target cells (Moran et al. 2001; Watson et al. 2003). Thus, environmental redox status can regulate cell–cell interactions and ensuing adaptive responses via transcriptional and posttranscriptional mechanisms by induction of stress proteins, antioxidants, cell adhesion molecules, and activators of cell proliferations (Moran et al. 2001).

Glutathione/glutathione disulfide (GSH/GSSG) system has been defined as the major player in intracellular redox homeostasis (Moran et al. 2001; Watson et al. 2003). Reduced GSH acts directly as a ROS scavenger, is a substrate for detoxification enzymes, and reduces protein disulfides capable of regulating transcriptional and posttranscriptional cellular response. Some functions of the GSH system are likely dependent on GSH concentration in tissues, and others are dependent on the actual glutathione redox potential of the thiol-disulfide couple (Moran et al. 2001). The redox potential (E*h*) for GSH/GSSG in cells and tissues is considerably more reduced than for extracellular fluids, which are influenced by redox state of another -SH couple, cysteine/cystine (Cys/CySS) (Gorbunov et al. 2006). Recent data available for cellular and tissue E*h* values are in the range of −260 to −150 mV with a midpoint potential of approximately −250 mV. More reduced E*h* values have been defined for highly proliferating cells, whereas more oxidized values are present in cells undergoing apoptosis (Watson et al. 2003). Therefore, cellular displacement of GSH and influx of Cys during tissue trauma could themselves trigger a metabolic switch that can initiate tissue remodeling.

This report will illustrate the correlation between the BSW-induced oxidative stress and the antioxidant balance in the lung and peripheral blood and the activity of redox-sensitive metabolic pathways involved in posttraumatic recovery.

METHODS

Experimental Studies of Primary Blast Lung Injury

In order to study the effects of blast exposure in the laboratory, we generated simulated BSW using a compressed air-driven shock tube shown in Figure 8-1 that was developed based on a concept described earlier (Cassen et al. 1950; Celander et al. 1955; Richmond et al. 1961b).

Basically, the shock tube used is a horizontally mounted 533 cm long, 30 cm diameter, circular steel tube divided into two chambers: a 76 cm (2.5 feet) compression chamber and a 457 cm (15 feet) expansion chamber separated by one or more polyethylene Mylar™ diaphragms (DuPont Co, Wilmington, DE) of specific thickness. Air is pumped into the compression chamber until the Mylar diaphragm is ruptured, generating a shock wave of specific magnitude depending on the Mylar sheet thickness followed by a rarefaction wave propagated down the expansion chamber. The peak pressure at the muzzle of the expansion chamber is measured by a

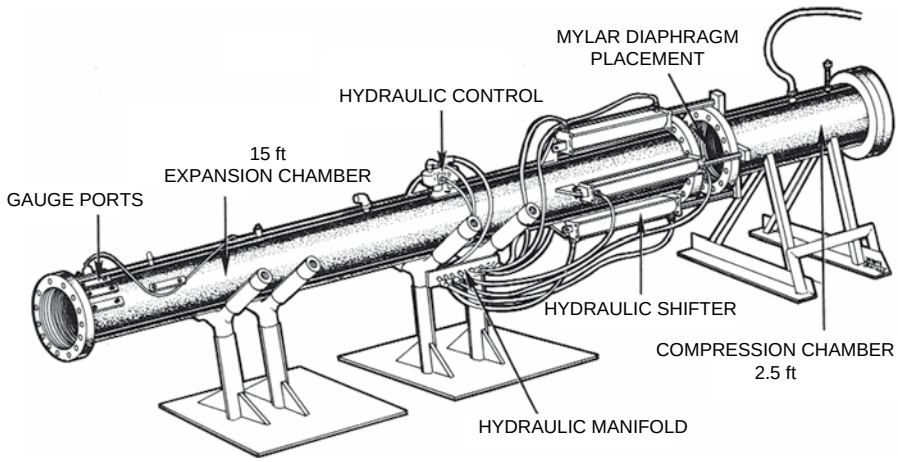

FIGURE 8-1
A schematic drawing showing the compressed air-driven shock tube used to simulate blast shock waves in the laboratory.

piezoresistive pressure-time (impulse) gauge (PCB 102M152, Piezotronics, Inc, Depew, NY). Similar gauges are placed at different locations along the expansion chamber to provide information about the BSW as it travels along the expansion tube. Each gauge uses an acceleration compensated quartz piezoelectric element coupled to a source follower, connected to a 12 channel signal power conditioner (PCB 483A10). The output is displayed on a digital oscilloscope and recorded (440, Nicolet Instruments, Corp., Madison, WI). A typical blast signature of a simulated blast overpressure wave generated in the laboratory using the shock tube is shown in Figure 8-2. The histogram presented in Figure 8-2 shows the positive (overpressure) and the negative (underpressure) phases, and the duration of the positive phase or the A-duration. Other devices used to generate BSW include the shock-wave lithotriptor (Jaffin et al. 1987; Pode et al. 1989).

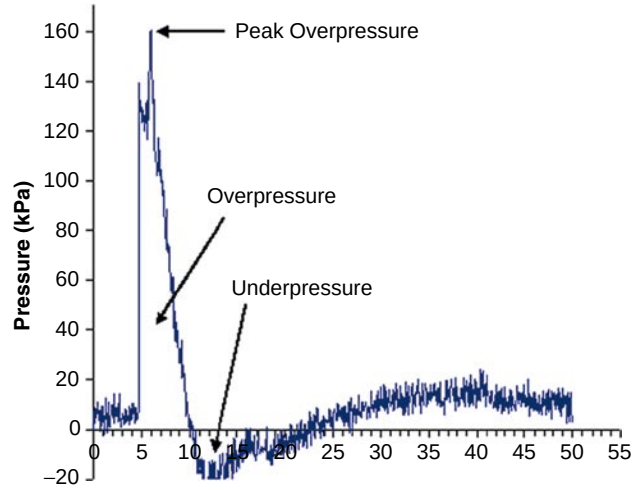

FIGURE 8-2
A histogram illustrating the pressure-time history (signature) of a typical shock wave (SW). The data represent an average of 10 randomly selected records of SW impacts producing lung injury at a moderate level. Peak overpressure, positive and negative phases of the SW are indicated with arrows.

Different animal models were used in our blast studies, including rats, guinea pigs, rabbits (whole body exposure), and sheep, pigs, and goats (localized exposures). The experimental animals were used always while deeply anesthetized and were euthanized before regaining consciousness to prevent potential pain from the exposure. Several analytical techniques outlined briefly next were applied to study the effects of blast exposures.

Electron Paramagnetic Resonance (EPR) Techniques

Low-temperature Electron Paramagnetic Resonance (EPR) spectroscopy of blood and lung tissue was used as described previously (Gorbunov et al. 1997; Osipov et al. 1996). Frozen samples of tissues or blood were assayed using an X-band EMX EPR spectrometer (Bruker Instruments, Inc. Hmb. Germany) or JOEL-RE1X (X-band) spectrometer (JOEL Instruments, Tokyo, Japan) fitted with a variable temperature controller (Research Specialists, Chicago, IL). The recorded EPR spectra were analyzed using WINEPR program package (Bruker Instruments, Inc. Hmb. Germany). Preparation of the frozen sample casts is described in detail elsewhere (Elsayed et al. 2000).

Bronchoalveolar Lavage (BAL) Analysis

Bronchoalveolar lavage (BAL) fluid samples were obtained from the lung *in situ* through the trachea after incision in the neck following euthanasia. The lungs were lavaged with 3 ml volume of Dulbecco's Phosphate Buffered Saline (DPBS) (pH 7.4) through a cannula inserted into the trachea. Cell pellets were pooled from the lavages and centrifuged at 1,200*g* for 10 min. The supernatants were collected and frozen immediately in liquid nitrogen, and stored at 80 °C until analyzed for the amounts of NO-derived products (N-oxides).

Chemiluminescence Analysis of N-Oxides

Analysis of NO-derived products (N-oxides) in the BAL fluid samples was conducted with a nitric oxide analyzer NOA 280 (Sivers Instruments, Inc., Boulder, CO). The assay is based on detection of the chemiluminescence generated from reaction of ozone with NO, which is catalytically produced from the end-products of NO-pathway [i.e., nitrites (NO_2^-), nitrosothiols (RSNO), and nitrates (NO_3^-), collectively defined as NOx]. The recorded chemiluminescence signals were analyzed using NO Analysis Software (Sivers Instruments, Inc., Boulder, CO).

Lung Tissue Preparations for Biochemical Analyses, Histology, and Immunofluorescence Microscopy

Immediately after exposure, the animals were euthanized, a thoracotomy performed, and the lungs extracted *en block* rinsed with ice-cold saline, blotted dry on filter paper, and weighed. After recording whole lung weights, an intact lung lobe was selected for EPR spectroscopy and frozen in liquid nitrogen at −176 °C as described in detail previously (Shinomiya et al. 1998;

Elsayed et al. 2000). The remaining lung lobes were weighed again then homogenized in five to 10 volumes of an ice-cold medium containing 20% glycerol, 50 mM KCl, 0.1 mM EDTA, 0.1 mM phenylmethylsulphonylflouride (PMSF), and 10 mM HEPES, pH 7.2, using a Polytron® homogenizer (Kinematika GmbH, Luzern, Switzerland), and used for antioxidant and lipid peroxidation determinations. Lung tissue samples from other animals were collected at necropsy, fixed in 4% buffered paraformaldehyde (pH 7.4), and embedded frozen in O.C.T. (optimum cutting temperature) embedding compound, and subjected to cryosectioning. The specimens obtained (10 μm sections) were stained with hematoxylin and eosin (H&E) for histological examinations or processed for immunofluorescence analysis with light, or fluorescence confocal microscopy, respectively.

Determination of Endogenous Antioxidants

Total thiols was determined by Ellman's assay as described earlier (Shinomiya et al. 1998), using 5,5′ -dithiobis [2-nitrobenzoic acid (DTNB; Ellman's reagent)] to determine protein sulfhydryls' contribution to the total DTNB-titrable thiol pool. The water-soluble antioxidants ascorbate and total thiols were determined by an EPR assay shown to be sensitive to oxidative stress (Simoni et al. 1995) as described previously (Gorbunov et al. 1997). This method is based on the concept that water-soluble antioxidants such as ascorbate and GSH are capable of donating electrons (hydrogen atoms, H) to phenoxyl radicals (Ph-O$^{\bullet}$) regenerating the phenols, and becoming oxidized in the process:

$$\text{Ph-O}^{\bullet} + \text{AH} \rightarrow \text{Ph-OH} + \text{A}^{\bullet}$$

Vitamin E (α-tocopherol), a lipid-soluble antioxidant, content was determined by the method of Lang et al. (1986). In that method, protein was precipitated in an aliquot of lung tissue homogenate using 10% acetic acid, centrifuged and the supernatant used for HPLC analysis of α-tocopherol as described previously (Elsayed et al. 1996).

Estimation of Lipid Peroxidation

Lipid peroxidation was estimated both as conjugated dienes and as fluorescent lipid peroxidation end-products. Conjugated dienes in lipid extracted from lung tissue homogenate by the method of Folch et al. (1957). The lipid extracts were evaporated under N_2 and the lipid dissolved in a mixture of methanol:hexane, 5:1 v/v. Conjugated dienes were estimated

spectrophotometrically at 232 nm as described by Recknagel and Glende (1984), and the results presented as the ratio of absorbencies at 232 and 215 nm. Fluorescent lipid peroxidation end-products were determined in the methanol:hexane extract by measuring the fluorescence at 360 nm excitation and 400–550 nm emission (Trombly & Tappel 1975).

Staining for Catabolic Products of Extravasated Hemoglobin

Lung specimens (6 μm sections) fixed in 0.5% glutardialdehyde in PBS were stained with eosin, or Buffalo Black NRB reagent for hemoglobin, or Mallory reagent for iron to reveal a spatial localization of iron-containing complexes. Counterstaining was conducted with Gill #3 hematoxylin or nuclear red solution. The specimens were analyzed with Olympus AX 80 microscope equipped with objective lenses (20x, 40x, and 100x). Optical images were recorded with DP 70 color digital camera.

Immunoblot Analysis

Alterations in the amounts of HO-1, MPO, and Cu,Zn-SOD in lung hemorrhagic lesions were assessed using immunoblot techniques followed by protein separation in polyacrylamide gels. The primary antibodies used for hybridization were mouse anti-heme oxygenase-1 monoclonal IgG (Stressgen Biotechnologies, Victoria, BC, Canada) at 1:1000 dilution, rabbit anti-myeloperoxidase polyclonal IgG (Calbiochem, San Diego, CA) at 1:500 dilution, rabbit anti-Cu/Zn superoxide dismutase polyclonal IgG (Stressgen Biotechnologies, Victoria, BC, Canada) at 1:1000 dilution, and rabbit anti-transferrin polyclonal IgG (Innovex Biosciences) at 1:1000 dilution. Protein bands were identified by comparison with a molecular weight marker (Bio-Rad Laboratories Inc., Hercules, CA). β-Actin was probed to monitor equal loading. Semi-quantitative assessment of immunoblots was conducted using imageJ processing software (http://rsb.info.nih.gov).

Immunofluorescence Techniques and Image Analysis

The obtained lung specimens (see earlier) were processed for the immunofluorescence imaging as described previously (Gorbunov et al. 2000). The primary antibody against (1) HO-1 (rabbit polyclonal IgG from Stressgen Biotechnologies, Victoria, BC, Canada), (2) MPO (rabbit polyclonal IgG from Calbiochem, San Diego, CA), and (3) Cu,Zn-SOD (rabbit polyclonal IgG from Stressgen Biotechnologies, Victoria, BC, Canada) were used in 1:250 dilution in buffer A. This was followed by three additional

washes with buffer A and incubation with secondary fluorochrome-conjugated antibody and/or streptavidin-AlexaFluor 610 conjugate (Molecular Probes, Inc., Eugene OR), and with Heochest 33342 (Molecular Probes, Inc., Eugene OR) diluted 1:5000. The secondary antibodies used were (1) ALEXA 488 conjugated rabbit anti-goat IgG (Molecular Probes Inc., Eugene OR), (2) Cy2 conjugated goat anti-rabbit IgG (Rockland Inc., Gilbertsville PA), and (3) Cy3 conjugated donkey anti-mouse IgG (Rockland Inc., Gilbertsville PA). Processing and analysis of digital images were conducted using SimplePCI High Performance Imaging software (Compix Inc., www.cimaging.net) and ImageJ software (http://rsb.info.nih.gov).

RESULTS AND DISCUSSION

Oxidative Stress

To assess the antioxidant/pro-oxidant equilibrium in lung and blood after blast exposure, a number of biomarkers of oxidative stress were determined. They included tissue contents of a number of antioxidants (ascorbate, total protein thiols, and glutathione), and the ability to scavenge peroxyl radicals (a measure of endogenous antioxidants), total antioxidant reserve, and lipid peroxidation. The results of two studies (Elsayed et al. 1996; Gorbunov et al. 1997), are summarized in Table 8-2, where the data indicate conclusively that oxidative stress indeed occurs as a result of blast exposure.

Table 8-2 Changes in Biomarkers of Oxidative Stress Following Blast Exposure

Exposure	Ascorbate[a]	α-Tocopherol[a]	Total Thiols[a]	Reduced Glutathione[a]	Lipid Peroxidation End Products[a,b]	Conjugated Dienes[c]	Met H[a]	Total Antioxidant Reserve[d]
Control	1.46±0.12	1.00±0.11	70.5±5.6	13.73±2.16	2.60±0.41	0.285±0.018	22.1±14.5	14.83±0.67
Blast	0.68±0.13	0.70±0.05	51.7±2.0*	1.18±0.88	6.63±0.90	0.330±0.011	50.3±12.3	8.062±0.68
Change (%)	–53%*	–30%*	–27%*	–91%*	+155%*	+16%*	+128%*	–42%*

Data from Elsayed et al. (1996) and Gorbunov et al. (1997).
**= Statistically significant, n=6, P<0.05.*
[a]*Units were nmol/mg protein.*
[b]*Fluorometric determinations at 360 nm excitation and 400–550 nm emission (Pode et al. 1989).*
[c]*Arbitrary units as the ratio of absorbance at E_{235} nm/E_{215} nm.*
[d]*Delay in 2,2′-azobis-2-methyl-propanimidamide, dihydrochloride (AAPH)-induced chemiluminescence of luminol (minutes).*

The association between oxidative stress, ascorbate, α-tocopherol, and other antioxidant depletion in plasma after head trauma was reported in both experimental animals and in humans (Elsayed et al. 1996; Pietronigro et al. 1983; Shohami et al. 1999; Polidori et al. 2001; Bayir et al. 2002; K1ymaz et al. 2007). In addition, glutathione depletion was found to affect the immune function (Dröge & Breitkreutz 2000), impair survival in immunodeficient patients (Herzenberg et al. 1997), modulate gene expression in HepG2 cells through activation of protein kinase C alpha (White et al. 2005), and be required for proper function of certain T-cell systems (Kinscherf et al. 1994). The relationship between compromised immunity and blast-induced injuries is further complicated when it is accompanied by penetrating wounds acquired in battlefield during combat and in the cities from terrorist bombings, because it can lead to infections and sepsis (Peleg et al. 2004; Covey 2006).

Hemorrhagic Lung Injury and Turnover of Pro-oxidants

To fully understand the basis for the biochemical changes, we examined the histologic and immunohistochemical changes occurring in the lung after blast exposure. The most consistent lung lesions that occurred after exposure to a BSW at peak overpressure of 118 ± 7 kPa were bilateral diffuse parenchymal hemorrhages that involved the entire thickness of lobes compared to controls as shown in Figure 8-3.

The histopathologic lesions were characterized by massive extravasations of blood components that decomposed over time.

Leukocyte sequestration and transmigration had a focal character and were restricted mostly to the hemorrhagic foci. The phagocytic leuko-

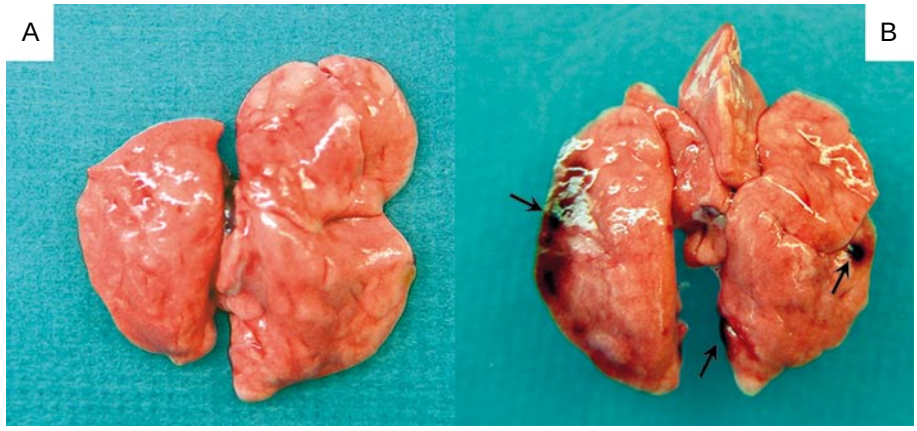

FIGURE 8-3
*Representative macroscopic views of lungs from a sham-treated (control) rat **(A)** and SW-exposed rat **(B)** 24 hr after exposure to a SW at peak overpressure of 118 ± 7 kPa. Arrows in **(B)** indicate hemorrhagic lesions.*

cytes (PhLC) contributed substantially to biodegradation of extravasated RBCs, and PMNs attached to RBC in clots were readily observed at ~3 h postexposure. Alveolar sequestration of PhLC was accompanied by deposition of the PhLC-released myeloperoxidase (MPO) (see Figure 8-4), which has been identified recently as "footprints" of PhLCs in the extracellular matrix and as a promoter of oxidative stress (Baldus et al. 2004).

The following period of observation (3 h–56 h) was characterized by destruction of extravasated RBCs. The RBCs were reduced in size and released Hb that partially appeared at 3 h post-exposure in the form of crystalline nano-particles (see Figure 8-5).

In conjunction with this effect a deposition of stainable Hb and catalytically active nonheme iron were observed in phagocytes and parenchyma cells that increased progressively during the following 56 hours (Gorbunov et al. 2006). At this stage, a formation of slender crystals with positive staining for Hb was observed on the septal surface and alveolar space. In some cases, these crystalloid structures covered the entire alveolar walls (see Figure 8-5C, indicated with arrow). These events occurred along with extensive erythrophagocytosis and erythrocyte biodegradation by resident macrophages in the lung (Gorbunov et al. 2004, 2006). The degradation of Hb proceeds via the heme oxygenase-dependent pathway and results in the formation of a variety of iron complexes in the lung available for Fenton-type reactions (see Figure 8-6). The amount of these complexes in the lesions can increase up to 5 μM compared to less than 0.1 μM in sham-treated rat lungs.

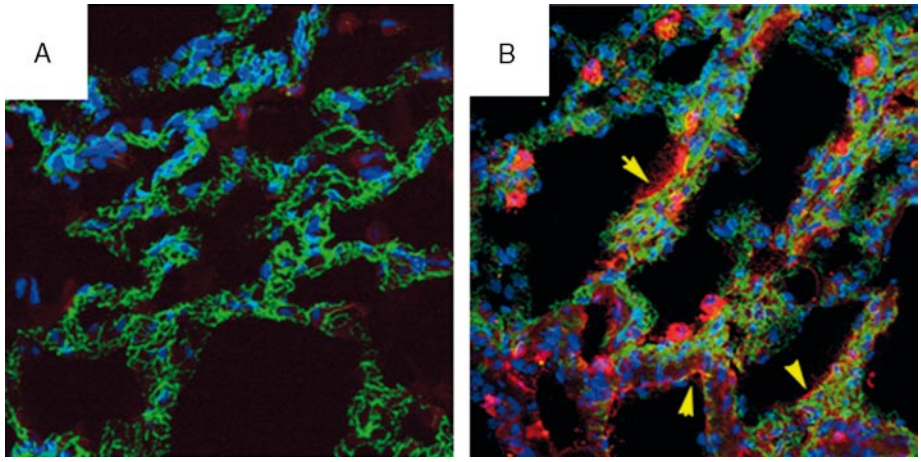

FIGURE 8-4
*Assessment of infiltration of myeloperoxidase (MPO)-abundant leukocytes and deposition of pro-oxidant MPO into alveolar septa in lung subjected to SW-exposure. Immunofluorescence images of VE-cadherin (green), a marker of vascular endothelium, and MPO (red) are shown in **(A)** (sham) and **(B)** (3 h post-exposure). An appearance of the MPO immunoreactivity in alveolar septa in hemorrhagic lesions due to degranulation of leukocytes is indicated by arrow in **(B)**. Note blue is counterstaining with Hoechst 33342.*

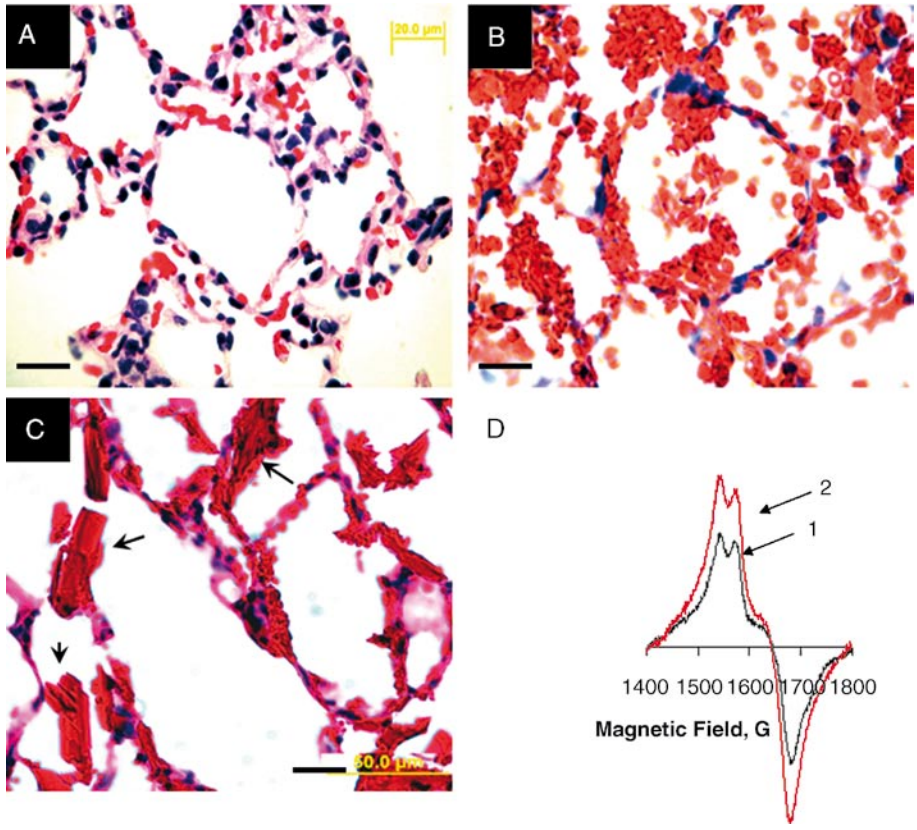

FIGURE 8-5
*Histological and electron paramagnetic resonance (EPR) assessment of the hemorrhagic lesions induced by impact of shock waves. Section from a sham-treated rat lung **(A)**; Section from a SW-exposed lung, 1 hour post-exposure **(B)**; Section from a SW-exposed lung, 24 hours post-exposure (solid phase hemoglobin formations are observed in the alveolar septa; indicated with arrows). Electron paramagnetic resonance spectra of transferrin obtained from the peripheral blood before (1) and 30 min after (2) shock wave impact **(D)**. Increased heme-free iron in blood following SW exposure was determined by the increase in the intensity of the transferrin signal.*

As a result, increased iron metabolism in the lung has been proposed to be one of the characteristics of hemorrhagic blast lung (Gorbunov et al. 1997, 2004, 2005; Elsayed et al. 1997b). Activation of iron turnover in the lesions involves transferrin and iron transporting systems in the lung cells, and results in increased concentration of nonheme iron in the peripheral blood within the first hour postexposure (see Figure 8-5). These effects were accompanied by increased EPR signals of free radicals (g = 2.008) in the lungs of treated animals (*versus* sham) (Elsayed 1997b).

A compensatory response to the microcirculatory insult in the lung was accompanied by systemic hypotension and release of nitric oxide (NO) in the lung detected using EPR spin-trapping techniques (Gorbunov et al. 2007). Thus, the amount of HbNO in the peripheral blood at 3 hr observations was $2.4 \pm 0.3\,\mu M$ (BSW-exposure), whereas in sham-treated animals this parameter did not exceed $0.8 \pm 0.2\,\mu M$ ($p < 0.01$, $n = 5$) (Gorbunov et al. 2007). This event, along with the PhLC-released NO, MPO, and

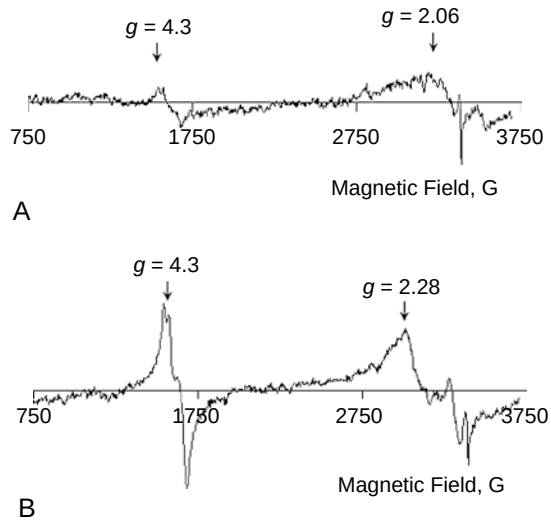

FIGURE 8-6
Formation of iron complexes in lung hemorrhagic lesions assessed using low-temperature EPR spectroscopy. ***(A)*** *EPR spectrum obtained from a sham-treated rat lung (note the appearance of EPR spectral components from blood [Fe3+] TRF complexes g = 4.3 and [Cu2+]-ceruloplasmin g = 2.06).* ***(B)*** *EPR spectrum obtained at 12 hr post-exposure indicating increased intensity of the EPR signals: [Fe3+] TRF complexes at g = 4.3, and appearance of low-spin iron (d3Fe3+) at g = 2.28 occurring due to decomposition red blood cell hemoglobin.*

catalytically active iron in aerobic conditions, create a particular environment for nitration of crucial proteins in the injured alveoli and thus, promote oxidative stress.

Oxidative stress also induces a number of adaptive cell responses driven by redox signaling cascades. We further investigated whether redox-sensitive elements known to be mediators of redox signaling of the inflammatory response (i.e., thioredoxin (TRX), NFkB, Ref-1, and Nrf2) were affected in our lung injury models. The redox-dependent induction of these factors was shown to be associated with their nuclear translocation (True et al. 2000; Matthews et al. 1992). This redox transcriptional response could drive adaptive responses essential for remodeling and recovery. Thus, in this model of blast lung trauma we have observed increases in the nuclear translocation of p50/p65 NFkB subunits along with TRX and Ref-1 (see Figure 8-7) within 3 hr post-exposure (Gorbunov et al. 2006).

Moreover, evidently nuclear translocation of TRX and Ref-1, and the TRX-dependent reduction of Ref-1 in the nuclear sphere are prerequisites for activation of a number of redox-sensitive transcriptional factors including NFkB (Nishi et al. 2002; Hedley et al. 2004). These effects were demonstrated recently using confocal immunofluorescence imaging and immunoblotting techniques (Gorbunov et al. 2007).

Moreover, immunoprecipitation of the nuclear fractions of p65 NFkB with subsequent immunobloting of the precipitated proteins for Ref-1 protein revealed an increase in the amounts of Ref-1/NFkB complexes in the

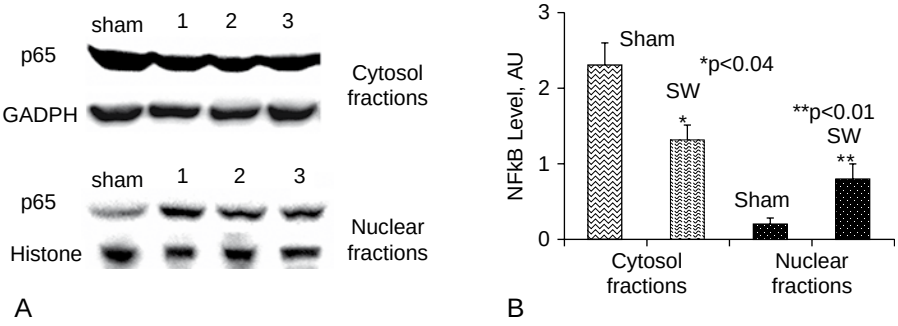

FIGURE 8-7
Immunoblot analysis of nuclear translocation of the NFkB transcriptional factor in alveolar cells of SW-exposed lungs. ***(A)*** *Representative immunoblot of NFkB p65 in the lung specimens from SW-induced injury (in triplicate: 1–3, versus respective sham-treatment).* ***(B)*** *Assessment of the alterations in fractional distribution of NFkB p65 induced by SW-exposure.* **Statistically significant with Tukey's test, p<0.05, relative to respective sham-treated.*

injured lung. We suggest that these events, including activation of nuclear translocation of TRX, Ref-1 and transcriptional factors NFkB and Nrf2, are parts of redox-sensitive signaling cascades activated by trauma-induced oxidative stress that are essential for further remodeling and recovery during trauma healing.

Compensatory Induction of Antioxidant System in Blast Lung

Compensatory response to the nitroxidative/nitrosative stress comprises a cascade of signaling reactions and the induction of stress proteins, which presumably help to maintain the redox homeostasis affected by the presence of pro-oxidants. We further assessed the status of HO-1 and Cu,Zn-SOD stress proteins, which suppress the level of superoxide anion radicals but are capable in promoting the Fenton-type reactions by releasing catalytically active [Fe] and hydrogen peroxide, an MPO substrate.

Cu/Zn-Superoxide Dismutase (SOD-1)

Immunoblot analysis showed that amounts of SOD-1 protein in lung hemorrhagic lesions changed in a time-dependent manner during 24 hr observation period (see Figure 8-8).

SOD-1 is an inducible stress-protein. However, it is constitutively present in many types of cells (including red blood cells and PhLCs) subjected permanently to oxidative stress, and protects them from excess superoxide anion radicals. Therefore, the dynamics of alterations in the SOD amounts in the injured lung reflected at least three different events: (1) immediate extravasation of blood (minutes after BSW impact), (2) immobilization of leukocytes in lung tissue (~1 to 24 hr after BSW impact), and (3) expression in the parenchymal cells (~ 12 through 24 hr after SW impact).

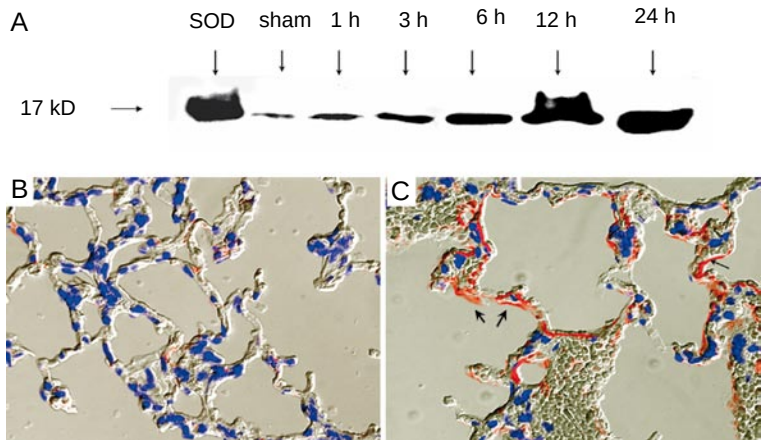

FIGURE 8-8
*Assessment of Cu,Zn superoxide dismutase (SOD-1) protein in lung hemorrhagic lesions induced by exposure to SW. Overlay of Nomarski images of alveoli and respective immunofluorescence images of deposition of SOD-1 protein (red) in lung alveolar septa of sham-treated **(B)** and injured lung at 24 hr postexposure. Note blue nuclei is counterstaining with Hoechst 33342.*

Heme Oxygenase Type 1 (HO-1)

Heme oxygenase type 1 (HO-1) is a stress-protein that can be induced by hemoglobin, transitional metals, and the oxidative and nitrosative stress via different signaling mechanisms including MAP kinases and Nrf2 (Numazawa et al. 2003; Kietzmann et al. 2003; Banning & Brigelius-Flohé 2005). The presence of extravascular Hb in inflammatory alterations create particular conditions for induction of HO-1 in hemorrhagic lesions. Therefore, it was not surprising to see a substantial difference in HO-1 immunofluorescence between sham-treated and injured lung, especially at late time points. Staining was evident in both leucocytes abundant with HO-1 and in the parenchymal cells (see Figure 8-9).

PhLCs and lung epithelial cells are considered to be major players in iron cycling in lung (Dennery et al. 2003). Therefore, HO-1 induction in these cells would be a valuable supplementation to erythrophagocytosis, and deposition of heme- and nonheme iron described earlier. Increased HO-1 protein in those areas occurred in a time-dependent manner, as revealed by immunoblot analysis. During the first 12 hr postexposure this increase was associated with transmigrated PhLCs (data not shown), and the following period of time was characterized by HO-1 elevation in alveolar cells.

CONCLUSIONS

Figure 8-10 summarizes the events we believe occur following exposure to the shock waves produced by an explosion and resulting in a primary blast injury to the lungs.

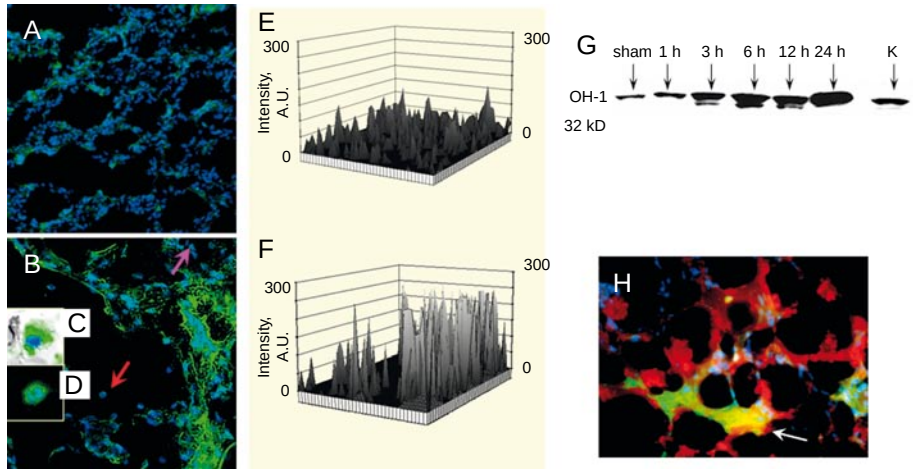

FIGURE 8-9 *Assessment of heme oxygenase protein (HO-1) in rat lung after exposure to blast shock wave. Projections of HO-1 (green) in alveolar septa of sham-treated* ***(A)*** *and SW-exposed lung at 24 hr postexposure* ***(B)****. Expression of HO-1 in macrophages (pink arrow) and PMN (red arrow) in* ***(B)*** *are shown in* ***(C)*** *and* ***(D)****, respectively, at magnification 100x. Note that PMNs were identified in the fluorescence images by the characteristic shape of PMN multinuclei after staining with Hoechst 33342.* ***(E)*** *and* ***(F)*** *3D profiles of HO-1 fluorescence intensity of the above immunofluorescence images, i.e.,* ***(A)*** *and* ***(B)****, respectively.* ***(G)*** *shows the immunoblot-analysis of HO-1 protein in lung hemorrhagic lesions at different time-points post-exposure, indicating HO-1 levels in sham-treated lung and noninjured lobes of SW-exposed lung* ***(K)****.* ***(H)*** *shows partial colocalization of HO-1 immunofluorescence (green) with 3-nitrotyrosine immunofluorescence (red) in lung alveolar septa at 24 hr postexposure Note: Colocalization of "green" and "red" is indicated with arrow. Blue nuclei are counterstained with Hoechst 33342.*

Basically, exposure to BSW resulting from an explosion can cause lung injury characterized by damage to alveolar air/blood barrier, pulmonary hemorrhage, edema, oxidative stress, and acute lung inflammation. Release of iron leading to oxidative stress occurring from blast exposure, resulted in blast-induced lung hemorrhagic injury, depletion of glutathione and other water- and lipid-soluble antioxidants causing a decline of the total pulmonary antioxidant reserve, which in turn is accompanied by increased oxidative injury. The adaptive response to redox stimulation in the injured lung was mediated at transcriptional and posttranscriptional levels by a number of redox-sensitive factors such as Nrf2, NFkB, thioredoxin, p38 MAPK, and so on. The observed adaptive response to blast injury resulted in the induction of a number of pro-inflammatory and anti-inflammatory proteins (e.g., ICAM-1 adhesion molecules, heme

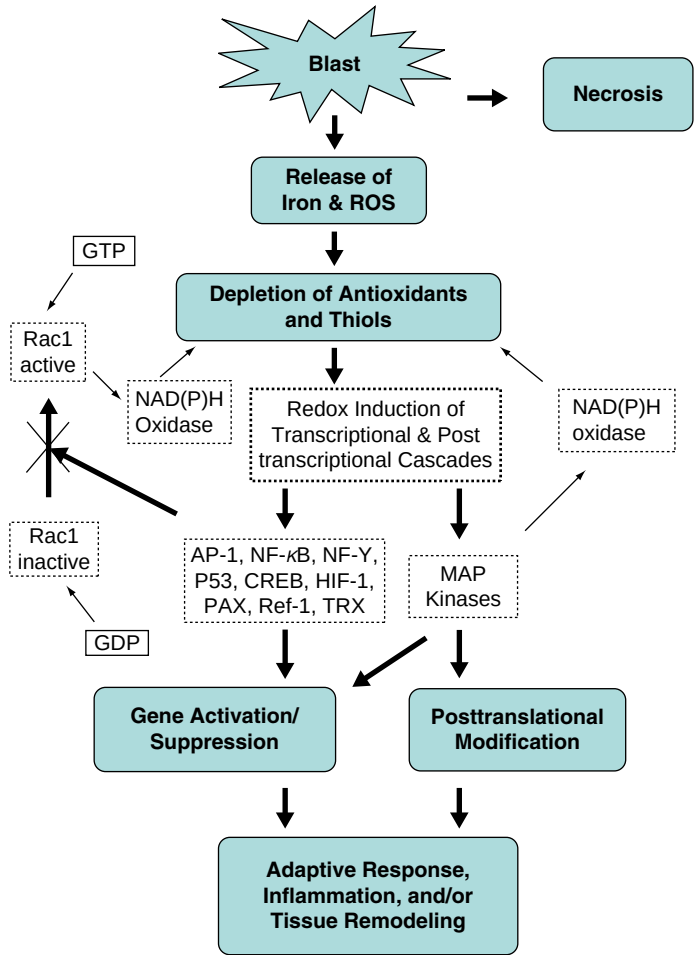

FIGURE 8-10
Summarizes the events we believe occur following exposure to the shock waves produced by an explosion and resulting in a primary blast injury to the lungs.

oxygenase 1), which may provide functional immunochemical homeostasis that illustrates the association of molecular and systemic level of homeostatic organization within the injured lung.

What is becoming apparent is that blast-induced injury is complex, involving a myriad of pathways and events. As we and others originally have proposed, blast injury is associated with free radical generation that releases iron, generates reactive oxygen and nitrogen species, alters the cellular redox potential, and produces oxidative stress. This in turn contributes to the induction of transcriptional and posttranscriptional cascades, and activation of pro-inflammatory alterations. These events further lead to gene activation and/or suppression and posttranslational modifications

ending either in adaptation marked by tissue remodeling and recovery or in inflammation, deterioration, and death. What is clear is that understanding the biochemical mechanism of blast-induced injury can lead the development of new treatment strategies that would support the trauma physician to better treat blast injury, and contribute to saving lives of blast victims. Toward achieving that goal, more funding resources have to be allocated and much more research still needs to be conducted.

ACKNOWLEDGMENTS

The studies described in this report were conducted under protocols approved by the Institute's Laboratory Animal Care and Use Committee in accordance with the Guide for the Care and Use of Laboratory Animals (NRC 1996). We thank Dr. Valerian Kagan for early collaboration and for the use of his JOEL EPR spectrometer in the early stages of research at the University of Pittsburg, and Ms. Jennifer Morris for operating the blast shock tube at Walter Reed Army Institute of Research.

DISCLAIMER

The views and opinions expressed herein are those of the authors and do not reflect those of the Department of the Army or the Department of Defense.

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CHAPTER 9

Inflammatory Response in Primary Blast Injury

Nikolai V. Gorbunov, Ludmila V. Asher, Nabil M. Elsayed, and James L. Atkins

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Summary
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INTRODUCTION

The damaging effect of shock wave (SW) resulting from explosions has been defined as a primary blast injury that may affect multiple internal organs without signs of external trauma (Maynard et al. 1988). The primary blast injury commonly is associated with numerous systemic

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abnormalities caused by the cardiopulmonary and neurogenic shock, and includes respiratory apnea, bradycardia, low cardiac index, arterial hypotension with insufficient compensatory vasoconstriction, and inflammation (Guy et al. 1998, 2000; Irwin et al. 1999; Gorbunov et al. 2005). These alterations, combined with pulmonary contusion, alveolar ruptures, and hemorrhage, result in ventilation-perfusion mismatch and progressive hypoxia, which along with pulmonary edema and inflammation could culminate in multiple organ failure (Guy et al. 1998, 2000; Irwin et al. 1999; Gorbunov et al. 2005). Physiological responses to blast trauma are accompanied by imbalanced release of paracrine and autocrine factors and neurohumoral mediators that compromise the molecular mechanisms supporting cellular and systemic homeostasis (Maynard et al. 1988; Guy et al. 1998, 2000; Irwin et al. 1999; Gorbunov et al. 2005). The resulting phenomenon can be defined as a blast-induced polytrauma. It is currently unclear whether the pathogenesis of this form of polytrauma differs from those of different etiology or not. Our main objective in this chapter is to discuss one aspect of this multifactorial question by describing the inflammatory response to blast-induced pulmonary hemorrhagic trauma.

MODEL OF BLAST LUNG TRAUMA

Exposure to the Experimental Shock Wave

The presented model of blast lung trauma has been described in our recent publications (Gorbunov et al. 2005, 2006, 2007). To simulate air blast SW in experimental conditions, we used a compressed air-driven shock tube consisting of a horizontally mounted, 12-inch-diameter, 15-foot-long steel expansion chamber separated from a 2.5-foot compression chamber by 0.12 mm and 0.25 mm thick polyester Mylar films (DuPont, Wilmington, DE). The shock wave was generated in the expansion chamber after rupture of the membrane produced by raising air pressure in the compression chamber. The dynamics of the pressure of the generated SW was determined by a piezoresistive gauge specifically designed for pressure-time measurements (model 102M152, Piesotronics, Depew, NY), which was placed at the end of the expansion chamber. To induce the blast lung trauma, deeply anesthetized male Sprague-Dawley rats (300–350 g weight) were suspended (right sight on) at the nozzle of the expansion chamber and exposed to released SWs.[1]

[1]Animal handling and treatments were conducted in compliance with the Animal Welfare Act and other federal statutes and regulations related to animals and experiments involving animals, and adheres to principles stated in *The Guide to the Care and Use of Laboratory Animals, National Research Council*, NRC Publication, 1996 ed. The facilities are fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

Gross Pathology and Evaluation of Blunt Trauma Injury

Injury score (IS) for SW-induced pulmonary trauma in rats was assessed using an injury scoring system developed recently for air blast-induced blunt trauma (Yelverton 1996). Briefly, the scoring system utilized a packet of scoring sheets to aid in assessment of lesions. Each sheet was designed to provide a quantitative assessment of the severity of the lesions in lung as defined by the equation:

$$IS = (E + G + ST)(SD)$$

where E, G, ST, and SD were defined as:

E extent of injury in terms of lung lobes (0–5 range)

G injury grade, which included the extent of surface area of the lesions (0–4 range)

ST severity type element, which classifies the type of the worst-case lesions (i.e., petechiae, punctures, ruptures) (0–5 range)

SD severity depth element, which indicates the depth of disruption of the worst-case lesion (1–4 range)

The severity of injury index (SII) was then calculated as: IS/Maximum Possible IS for rat lung (i.e., "56"). Thus, the assigned lung SII was 0.0 for "negative injury level," 0.03 through 0.04 for "trace injury level," 0.05 through 0.21 for "slight injury level," 0.22 through 0.36 for "moderate injury level," and 0.37 through 0.64 for "extensive injury level" (Yelverton 1996).

Tissue Sampling and Analysis

Arterial blood, lung, and bronchial-alveolar lavage (BAL) samples were collected to analyze inflammatory alterations induced by blast SW. BAL fluid samples were obtained through the trachea after incision in the neck following euthanasia. The lungs were lavaged with 3 ml volume of Dulbecco's Phosphate Buffered Saline (DPBS) (pH 7.4) through a cannula inserted into the trachea. Cell pellets were pooled from the lavages and centrifuged at 1,200 g for 10 min. The details of all bioanalytical techniques have been presented in our recent peer-reviewed publications (Gorbunov et al. 2005, 2006, 2007; Day et al. 2006).

Data were expressed as means ± S.E.M. Differences were evaluated by using one-way analysis of variance with Tukey's *post hoc* multiple comparisons test.

SYSTEMIC CARDIOPULMONARY ALTERATIONS IN SHOCK WAVE INDUCED INJURY

Based on our observations, the extent of the experimental blast lung injury is in a proportion to the amplitude of shock wave overpressure. As shown in Figure 9-1, the most consistent lung injuries produced by the generated SW were of "moderate" and "extensive" levels. Pulmonary contusion was accompanied by a short-term apnea and a significant circulatory suppression determined by a decrease in the both arterial blood pressure (AP) and heart rate (HR) within entire period of observation (i.e., 3 hours). These effects recently were described to be unique forms of pulmonary and cardiogenic shock and were associated with the increased vagal parasympathetic activity (Irwin et al. 1999). At the "moderate" injury, AP was 71 ± 7 mm Hg (versus 112 ± 8 mm Hg in sham) and HR was 228 ± 17 beat per min (versus 326 ± 28 beat per min in sham) that was correlated with increase in the blood levels of adducts of Hb with NO, a major vasodilator in blood (2.4 ± 0.3 μM HbNO versus 0.8 ± 0.2 μM; $p < 0.01$, n = 5) (see Figure 9-2A). These effects were even more pronounced at the "severe" hemorrhagic lung trauma—AP decreased to 44 ± 6 mm Hg and HbNO level in blood was 6.3 ± 1.1 μM (see Figure 9-2A, insets). The SW-induced circulatory suppression was attenuated substantially by N-methyl-D-glucamine dithiocarbamate (MGD), a NO-trapping agent, administered

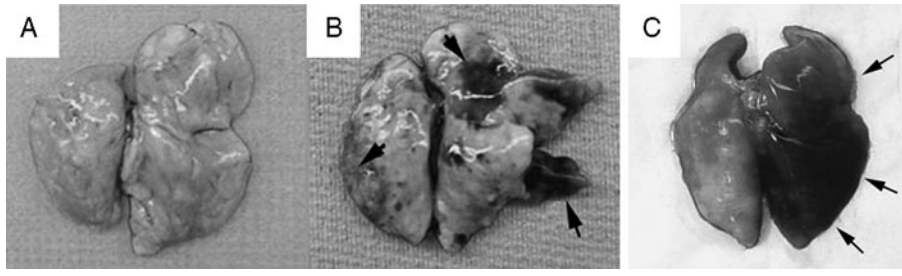


FIGURE 9-1 *Gross pathology of hemorrhagic lesions in lung after exposure to experimental shock wave.* ***(A)*** *Sham Treatment;* ***(B)*** *Moderate Injury;* ***(C)*** *Extensive Injury. Hemorrhagic lesions in the injured lungs are indicated with arrows.*

intravenously or via trachea. That was accompanied by accumulation of the NO-spin trap complexes in the injured lung (see Figure 9-2B).

Based on these observations we have concluded that suppression of cardiovascular activity induced by blast SW depends on the effective level of nitric oxide released in the vascular endothelium. In addition to its cardiovascular effects, such high levels of NO production could potentially promote coagulopathy, nitrosative and nitrative stress, leukocyte chemotaxis, and multiple organ failure. To date only the nitrative stress and leukocyte chemotaxis have been explored.

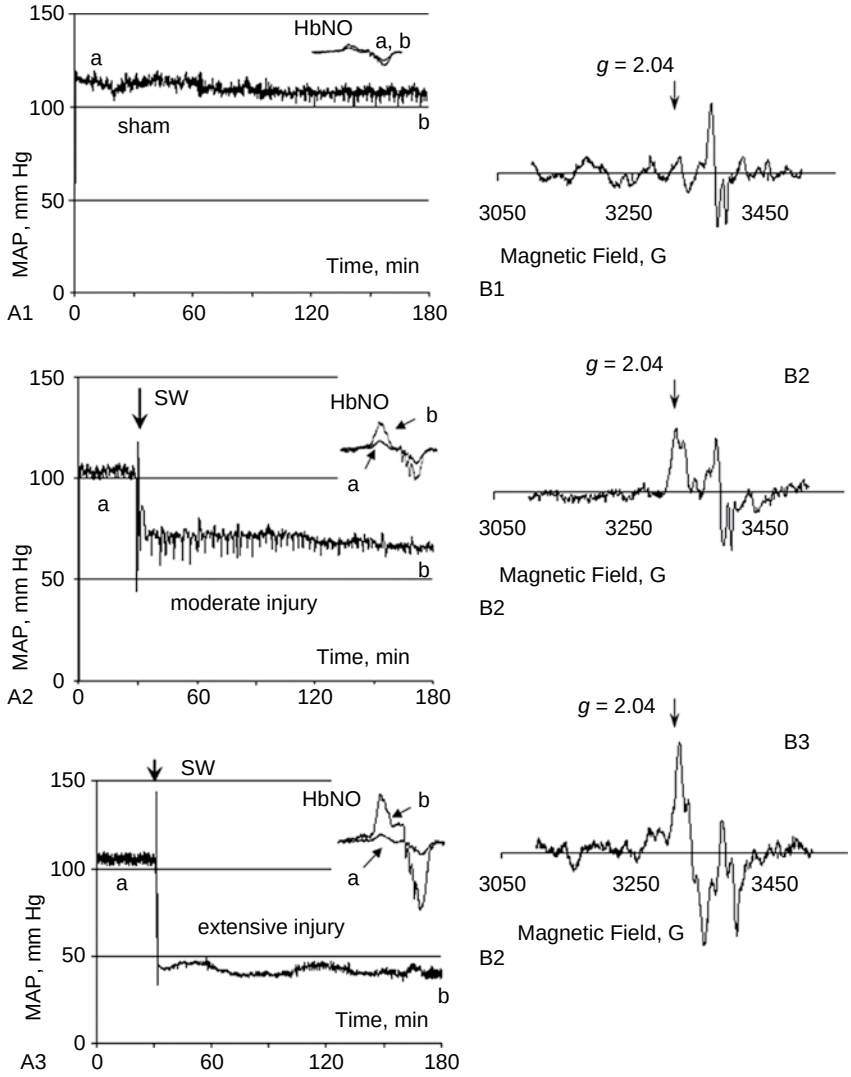


FIGURE 9-2

Graphs illustrating ***(A)*** *Alterations in time-course of Mean Arterial Blood Pressure (MAP) and* ***(B)*** *Associated increase in nitric oxide production in lung due to exposure to shock wave.* ***(1)*** *Sham Treatment;* ***(2)*** *Moderate Injury;* ***(3)*** *Extensive Injury. EPR spectra of HbNO in blood before treatments* ***(a),*** *and at the end of experiments* ***(b)*** *are shown in the insets 1, 2, 3 in the panel* ***A****. Representative low-temperature EPR spectra of NO adducts with* $(MGD)_2Fe^{2+}$*-spin trap (g = 2.04) in lung are shown in the panel* ***B****.*

SYSTEMIC AND LOCAL INFLAMMATION IN SHOCK WAVE INDUCED PULMONARY TRAUMA

SW-induced neurogenic and circulatory shock is followed by brisk release of inflammatory mediators, which evidently is sufficient for recruitment and activation of the resident and circulatory phagoctic leukocytes (Irwin et al. 1999; Gorbunov et al. 2005). The accompanying alveolar rupture and blood extravasation trigger the second cascade of pro-inflammatory events at systemic and local injury levels. We have assessed the resulting inflammatory alterations in the peripheral blood and the lung hemorrhagic lesions using (1) ELISA-based assays for cytokines/chemokines; (2) the flow-cytometry analysis for the circulatory PMNs; (3) electron paramagnetic resonance spectroscopy for sequestration of blood plasma iron; and (4) electron microscopy, immunofluorescence microscopy, and immunoblot analysis for leukocyte trafficking and inflammation in lung (Gorbunov et al. 2005, 2006, 2007).

Assessment of Macrophage Inflammatory Protein 2 (MIP-2), Interleukin IL-6, and Associated Iron Sequestration in Rat Blood Plasma

The rat chemokine MIP-2 (equivalent to human IL-8) is a highly selective chemoattractant of PMNs, and therefore is useful for prediction of the increase of PMN trafficking in injured lung. Alteration in MIP-2 status was monitored in the peripheral blood after exposure to SW. Levels of MIP-2 in plasma were elevated at 1, 3, and 6 hr following injury. Plasma MIP-2 increased from 2.9 ± 2.6 pg/mL in control rats, to 33.0 ± 7.9 pg/mL, 35.0 ± 7.3 pg/mL and 78.9 ± 20.5 pg/mL at 1 hr, 3 hr, and 6 hr, respectively, in injured rats.

The inflammatory response to SW injury was accompanied by pronounced hypoferremia in the peripheral blood that was determined by depletion of blood plasma iron-transferrin complexes, major carriers of iron in blood (Gorbunov et al. 2005, 2006, 2007). This effect was determined to be in a dose-dependent manner with severity of injury, and maintained within 56 hr observation period (Gorbunov et al. 2005, 2006, 2007). The maximal rate of decay of concentration of the iron-transferrin complexes in the arterial blood was observed within the first three hours postexposure. Thus, in the "moderate" injury the level of iron-transferrin decreased to $7.5 \pm 1.3\,\mu M$ (versus $19.7 \pm 0.6\,\mu M$ in controls, $p < 0.01$, $n = 10$) (see Figure 9-3).

The inflammatory hypoferremia is a common phenomenon of acute phase response in major trauma. It is considered to be a part of host defense mechanisms against opportunistic and aggressive infections. The acute phase sequestration of plasma iron in bone marrow may be essential for the acute phase activation of hemopoiesis and leukocyte maturation and is mediated by the acute phase IL-6–hepcidin axis (Jurado 1997; Ganz & Nemeth 2006). This is consistent with the increase in the concentration of IL-6 in the blood plasma after exposure to SW. Thus, the concentration of IL-6 in samples obtained from rats with moderate injury level was 408 ± 40 pg/mL, which was significantly higher than in sham-treated groups (24 ± 3 pg/mL, $p < 0.01$, $n = 15$). Substantial amounts of IL-6 (107 ± 29 pg/mL), IL-1β (3.4 ± 2.1 pg/mL), and MCP-1 ($1{,}485 \pm 414$ pg/mL) inflammatory chemokines were determined in BAL fluid of injured animals, whereas the concentrations of these chemikines in BAL fluid of the sham-treated animals were undetectable ($n = 6$). That was accompanied by release of CINC-2, a PMN chemoattractant, in the alveolar parenchyma of injured lung (see Figure 9-4).

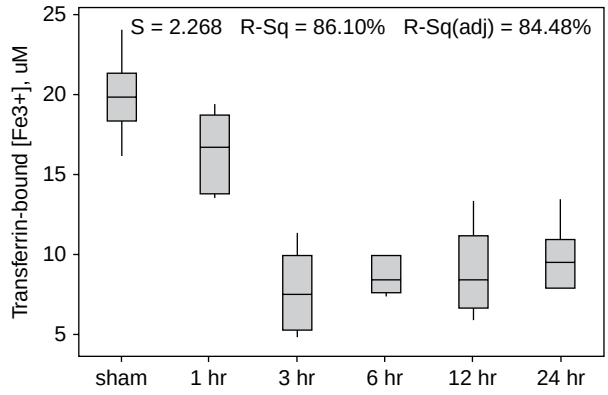


FIGURE 9-3
Amounts of iron-transferrin complexes in the rat peripheral blood at different time-points of post-exposure period. Moderate lung injury. Values are least squares means for concentration of $[Fe^{3+}]$TRF in box plots ranging from the 25th to 75th percentile. Bars indicate the 5th and 95th percentiles.

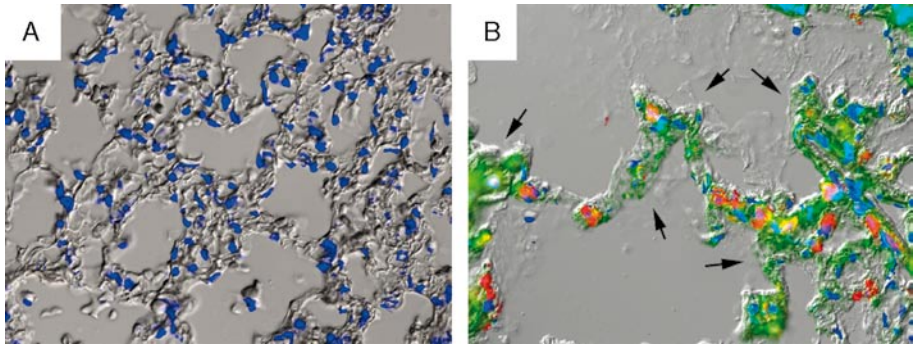


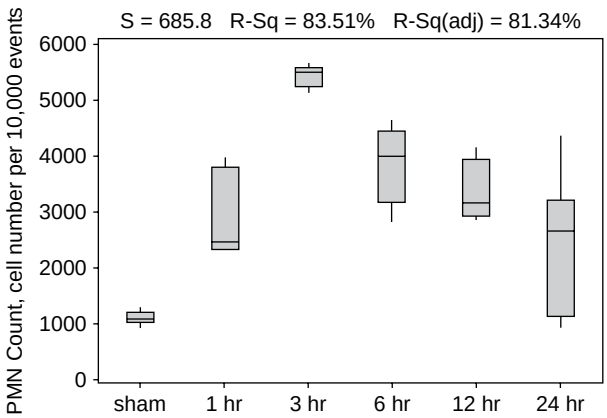
FIGURE 9-4 *Overlay of representative Nomarski and immunofluorescence images of lung specimens from sham-treated rat **(A)** and rat subjected to SW-induced injury at 6 hr following exposure **(B)**. Assessment of sequestration of granulocytic leukocytes in the alveolar capillary endothelium was conducted with immunostaining for CD11b adhesion molecules (Red, Alexa 610), and CINC-2 (Green, Alexa 488). Counterstaining for nuclei (Blue) was conducted using Hoechst 33342.*

Inflammatory Neutrophilia and Neutrophil Activation Induced by Shock Wave Exposure

Figure 9-5 shows that SW-induced moderate trauma was accompanied by rapid PMN recruitment to the peripheral blood. Neutrophilia occurred within the first hour following exposure as determined by increased neutropil (PMN) counts in blood samples using the flow-cytometry techniques. The number of PMNs in peripheral blood at this time increased from 1,090 ± 66 PMNs per 10,000 particles in the control group to 2,948 ± 359 PMNs per 10,000 particles in the injury group. PMNs in the blood of injured animals continued to increase at 3 hr postexposure to 5,458 ± 92 PMNs per 10,000 particles. A significant relative decrease of this effect occurred during the later time-points of observation (i.e., 6 hr, 12 hr, and 24 hr) (see Figure 9-5), which probably reflected PMN sequestration by target tissues. Still, the steady state counts of blood PMNs at 6 hr, 12 hr, and 24 hr following exposure remained significantly above control counts, at 3,850 ± 315 PMNs, 3,351 ± 293 PMNs, and 2,400 ± 442 PMNs per 10,000 particles (Gorbunov et al. 2006, 2007). The observed neutrophilia was accompanied by activation of PMNs determined by the increase in the expression of pro-inflammatory adhesion molecules (i.e., CD11b) on their surface. Thus, the augmentation of the CD11b immunofluorescence in PMNs increased progressively within the entire period of observation and was threefold higher than in the respective controls (Gorbunov et al. 2006, 2007).

FIGURE 9-5

Effect of SW Exposure on PMN counts in the peripheral blood at different time-points of postexposure period. Moderate lung injury.
Values are least squares means for PMN counts in box plots ranging from the 25th to 75th percentile. Bars indicate the 5th and 95th percentiles.



Microvascular Inflammation Induced in the Injured Lung

Progressive inflammatory neutrophilia in the SW-exposed animals resulted in the microvasclar sequestration and alveolar emigration of the phagocytic leukocytes (PhL) (i.e., PMNs and monocytes) from blood to the sites of the lung lesions. The sites of PhL infiltration were associated with hemorrhagic lesions produced by the SW impacts. It is likely that autocrine mediators, such as CINC-2 and reactive oxygen and nitrogen species, release from alveolar septa and participate in this coordination (Gorbunov et al. 2006, 2007). The dynamics of PhL infiltration was estimated by accumulation

of the myeloperoxidase (MPO) protein, a PhL-specific marker, in the inflammatory lesions. Thus, immunoblot analysis and immunofluorescence imaging of MPO showed time-dependent accumulation of MPO-containing cells in the lung specimens of the exposed animals (see Figure 9-6). These alterations were corroborated by light microscopy analyses of PhL of the lung specimens and BAL fluid (Gorbunov et al.

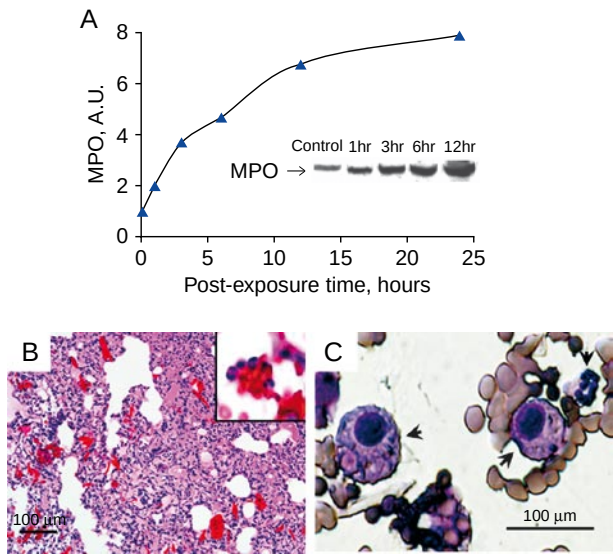


FIGURE 9-6 *Assessment of infiltration of the phagocytic leukocytes in hemorrhagic lesions of shock wave-injured lung.* ***(A)*** *Immunoblot assay of myeloperoxidase (MPO), a marker of phagocytic leukocytes, in hemorrhagic lesions at different time-points following SW exposure.* ***(B)*** *Histological examination of hemorrhagic lesions induced by SW impact. A massive infiltration of the phagocyte leukocytes followed by lysis of erythrocytes and alveolar cells, development of hemorrhagic edema, and a formation of solid phase hemoglobin (red clusters in* ***B****) were observed at 24 hr postinjury. Bar 100 µm. Magnification 20x. Inset is a magnified image of the infiltrated PMNs that are attached to fibrinogen on a blood clot in the injured alveolus. Magnification 100x, zoom 2x.* ***(C)*** *Light microscopy of cells collected in BAL fluid at 24 hr following SW exposure (HE staining). Macrophages performed erytrophagocytosis and PMNs are indicated with arrows. Magnification 100x, zoom 6x. Digital images were captured with DP 70 camera mounted on Olympus AX80 fluorescence microscope.*

2006, 2007). The observed inflammatory alterations in lesions were characterized by PMN degranulation and partial release of MPO into alveolar space and an appearance of MPO immunoreactivity observable in the alveolar septa at 3 hr postexposure. The intensity of MPO immunofluorescence in alveolar septa increased gradually in a time-dependent manner and was accompanied by the appearance of immunoreactivity against nitrated proteins indicating implication of nitric oxide and MPO in the inflammatory injury. The infiltrated PhL accelerated lysis of the extravasated erythrocytes and produced erythrophagacytosis (see Figure 9-6).

The diapedesis of the sequestered PhL in the alveolar microvasculature was synchronized with pro-inflammatory alterations in microvascular endothelium (Gorbunov et al. 2007). Indeed, the developed oxidative stress not only facilitated the PhL adhesion on vasculature—it also caused decrease on endothelial integrity provided by the VE-cadherin adhesion junctions, and promoted expression of the endothelial intercellular adhesion molecules type 1 (ICAM-1) that is essential for the increase in the microvascular permeability and diapedesis of PhL (Gorbunov et al. 2006, 2007). As shown in Figure 9-7, spatial coordination of the ICAM-1 expressed in the microvessels provided optimal configuration for effective "docking" of the inflammatory PhL. Indeed, the maximal immunofluorescence for ICAM-1 occurred at the lamellar protrusion of PhL outlining endothelium at the segments of transmigration. The estimated 3D colocalization of β_2-integrins and their counterreceptors (i.e., ICAM-1) in such "docking" constructs was $r \sim 0.9$ (Pearson correlation). These phenomena were accompanied by increase in the immunoreactivity of the lysosomal glycoprotein LAMP1 on PhL, which presumably facilitates the leukocyte transmigration (Kannan et al. 1996).

The electron microscopy analysis has shown that ultra-structural alterations in alveolar membranes could occur within first three following SW-impact (see Figure 9-8). The damage to the alveolar capillaries correlated with diapedesis and development of edema (see Figure 9-8A). That was accompanied by phagocytosis of erythrocytes, and massive release of hemoglobin in the alveolar space (see Figure 9-8B). In addition, numerous multilamellar bodies, representing extracellular surfactant, were present in alveoli suggesting damage to the type 2 alveolar epithelial cells (see Figure 9-8C).

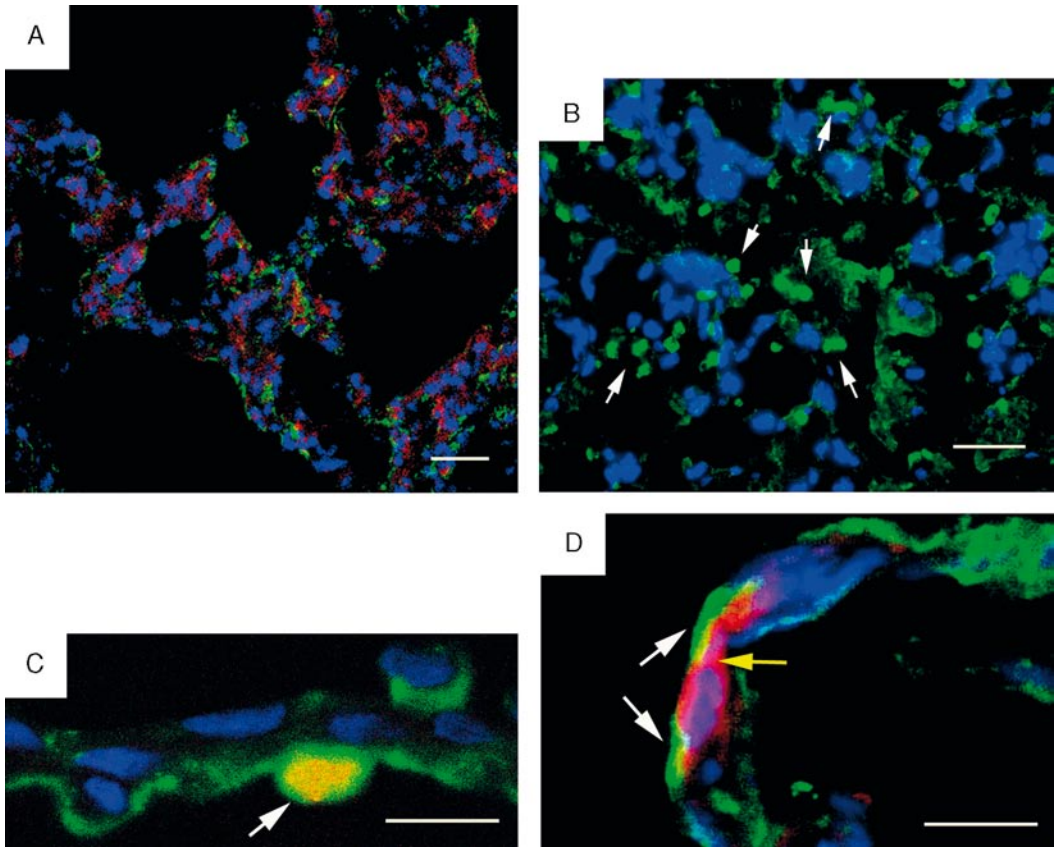


FIGURE 9-7

Projections of the ICAM-1 adhesion molecules (green channel) and α_M-integrins, markers of the pagocytic leukocytes (red channel), in the lung specimens from the animals subjected to shock wave exposure. ***(A)*** *Sham-treatment.* ***(B)*** *Three hours after exposure to SW. Magnification 60x, bar is 25 μm. Expression of ICAM-1 in the lung microvessels (green circles in* ***B****) is indicated with white arrows.* ***(C)*** *ICAM-1 projection in a magnified section of alveolar microvessel (indicated with white area) in a selected area of* ***B****. Bar is 10 μm.* ***(D)*** *Projection of spatial distribution of ICAM-1 (white arrows) in a microvessel "docking" pocket along with the polarized infiltrating leukocyte (yellow arrows). Bar is 10 μm.*

SUMMARY

Recent observations suggest that several different mechanisms are probably responsible for the various manifestations of pulmonary insufficiency developed in SW-induced trauma (Maynard et al. 1988). Thus, although the immediate pulmonary compromise is mostly characterized by exaggerated reflex responses (such as apnea, bradycardia, and arterial

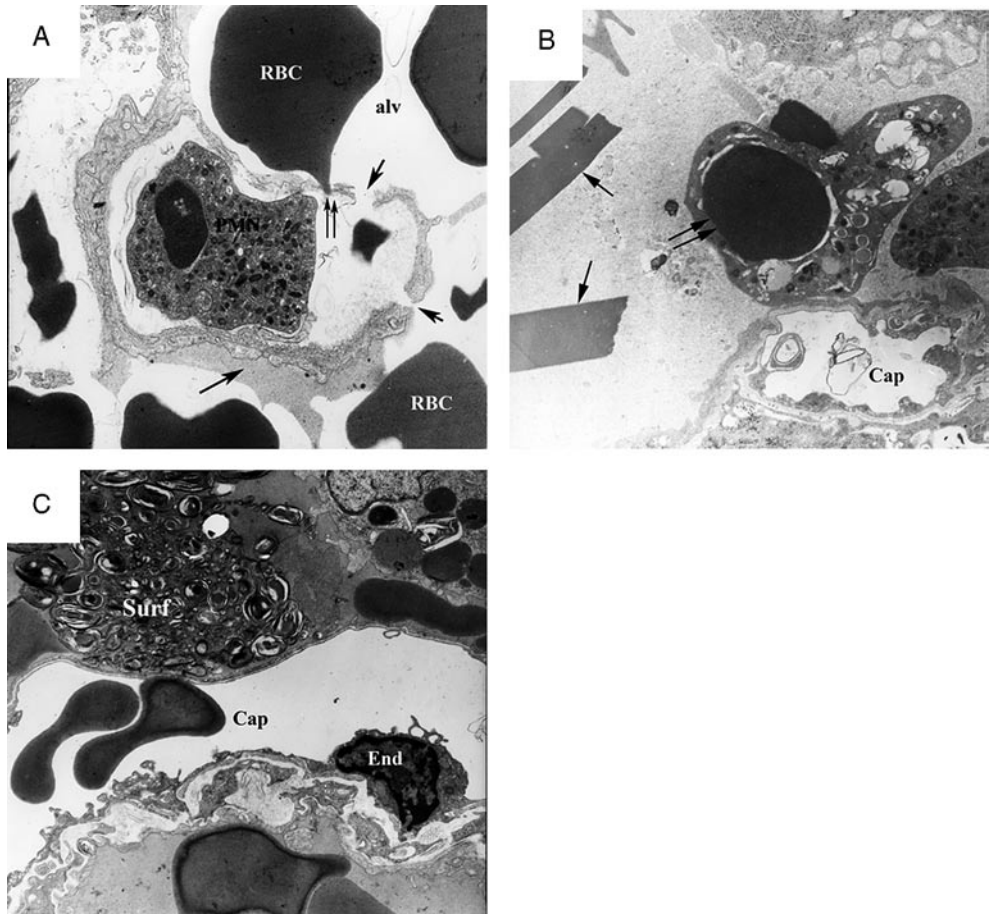


FIGURE 9-8

Electron micrographs of the rat lungs at 3 hours following exposure to shock wave. ***(A)*** *Alveolar edema with an intra-alveolar hemorrhage is present in the lung (arrow). Part of a capillary is damaged (arrows heads), and there is diapedesis of an erythrocyte through a capillary wall into alveolar space (double arrow). RBC, red blood cell, PMN, polymorphonuclear leukocyte, alv, alveolar space. Original magnification 17,000x.* ***(B)*** *Alveolar space contains several hemoglobin crystals (arrows) and a macrophage with a phagocytized RBC (double arrow). Cap, capillary. Original magnification 17,000x.* ***(C)*** *Accumulation of a large amount of extracellular surfactant in alveolar space (Surf) suggests an extensive damage to type 2 alveolar epithelial cells. Cap, alveolar capillary. End, endothelial cell. Original magnification 13,500x.*

hypotension), barotraumatic gas embolism, and internal bleeding, the delayed respiratory injury is likely due to the local and systemic alterations induced by the extravasated blood components (Maynard et al. 1988; Guy et al. 1998, 2000; Irwin et al. 1999; Gorbunov et al. 2005,

2006, 2007; Tsokos et al. 2003). The developed traumatic inflammation can orchestrate proteolytic and oxidative reactions, and lead to the functional derangements and morphological transformations. In spite of the fact that the clinical presentation of the blast lung trauma is well characterized and has been found to be similar in many aspects to those of blunt and hyperbaric trauma, its molecular pathophysiology remains for the most part unclear (Cernak et al. 1999).

Blast-induced inflammation is an essential phase of systemic response to support homeostasis altered due to cardiopulmonary and neurogenic shock, a mechanical tissue rupture, and extravasation of blood. As we have shown, the inflammatory response to cardiopulmonary injury is characterized by expression and increase in the systemic and local levels of pro-inflammatory mediators and chemoattractants that trigger both neutrophilia and inflammatory transformations in the vascular endothelium and the injured parenchymal cells. The following increase in vascular permeability and chemotaxis of the circulatory PhL in lung results in the lung cell repopulation and the inflammatory remodeling aimed at resolution and healing of the traumatic lesions (Gorbunov et al. 2005, 2006, 2007; Chavko et al. 2006).

The chemotactic PMNs are known to be in the first wave of migrating cells into injured tissues. These cells loaded with deadly enzymes are the first line of the cell protection against infections. However, a massive invasion and degranulation of the activated PMNs in the injured lung may cause severe pneumonia and acute respiratory distress syndrome.

Demargination and the acute release of PMNs from the bone marrow are critical steps in their trafficking to sites of inflammation. These processes are stimulated by systemically acting inflammatory mediators, such as the chemotactic chemokines (e.g., MIP-2) and nitric oxide. The further diapedesis and emigration of PMNs in the sites of injury is "navigated" by the locally released chemoattractants (e.g., CINC-2, ROS, RNS) and is facilitated by increased vascular permeability. A particular role in the PMN transmigration in the lung alveolar microvasculature is attributed to interplay of the PMN expressed integrines and their counterreceptors, ICAM-1, expressed on endothelium. Thus, a synchronous up-regulation of ICAM-1 and down-regulation of the adhesion junction VE-cadherin have been proposed recently to be essential for PMN harboring and diapedesis.

Many of these events also are seen in blunt trauma to the lung; however, there is also a systemic response to blast-induced lung injury that involves systemic release of neutrophils, production of inflammatory cytokines, and release of NO, which contributes to hypotension and bradycardia. It remains to be determined if these are unique features of blast-induced lung injury that may benefit from specific therapy.

ACKNOWLEDGMENTS

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DISCLAIMER

The views, opinions, and/or findings contained herein are those of the authors and should not be construed as an official Department of the Army position, policy, or decision.

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PART 4

Global Experiences of Blast Injury and Mass Casualty Management

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CHAPTER 10

Mass Casualty Events—Suicide Bombing: The Israeli Perspective

Limor Aharonson-Daniel, Gidon Almogy, Hany Bahouth, Zvi Feigenberg, Yoram Kluger, Kobi Peleg, Avraham I. Rivkind, and Boaz Tadmor

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The Epidemiology of Trauma Casualties
Methods
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INTRODUCTION

The last six years have enriched the Israeli comprehensive medical system enormously about ways and different solutions on how to cope with the challenges of the modern threat of mass casualty events arising from voluntary and civilian-targeted suicide bombers. We have learned how to deal with the continuum of care from the treatment on scene of the innocent bystander, to the delivery of care by the first responders through the coordinated evacuation phase, triage at different hospitals levels, to the hardship of rehabilitation. It does not mean only gaining more operational expertise, but also creating new concepts, changing a state of mind, and most importantly, a phase of learning how to manage this new type of knowledge in a very quick and efficient way. There are several basic elements that determine the damage to the human body:

- The body protection limits
- The amount of energy in the blast wave or front
- The direction of the front
- The environment (open, closed, confined)
- Knowing that the body's natural protection is limited and that no one is going to his or her everyday activities carrying a shield

In most of the bombs used, the terrorists added a new dimension by including metal elements in the form of nails, nuts, metal balls, and the like, for the purpose of creating even more devastating damage to the innocent casualties in the form of penetrating wounds in addition to the blast and shearing force injuries. This potential synergistic damaging effect mandated that the medical system at all levels had to find new innovative ways to think and to treat the patients in a multidisciplinary way. Emergency Medical Services (EMS), hospitals, rehabilitation facilities, and the patients themselves had to go through a very painful learning

curve in order to assimilate the new knowledge. In this chapter, we tried to assemble and present the most important new pieces of knowledge that we have collected during those years in the different phases of time and place in the continuum of care. We sincerely hope that this modest contribution will contribute to save lives wherever and whenever is needed.

This chapter is divided into four sections. The first section deals with the known mechanisms of injuries during a conventional bombing. The second section deals with the new concepts and lessons learned of the Israeli EMS system, the MAGEN DAVID ADOM. The third section presents the wisdom gained by the Trauma and Surgery division in a level 1 trauma center in Jerusalem. The forth section is an overview of the epidemiology and statistical analysis of the casualty population and the administrative and logistic burden on the hospitals.

MECHANISM OF INJURY IN BOMB EXPLOSIONS

Terror takes many forms, but in general, the common denominator is the calculated use of violence or the threat of violence to attain political, religious, or ideological goals. The number and extent of worldwide suicide attacks has risen sharply in recent years (Eisman 2001; Karmy-Jones et al. 1994; Slater & Trunky 1997). Bombing attacks directed against innocent civilians have become the primary weapon of terror groups and rapidly emerged as a worldwide epidemic. They have been perpetrated in many and diverse locations and apparently no community is immune. With the exception of the chemical incidents in Matsumoto (Slater & Trunky 1997) and the Tokyo subway (Okumura et al. 1998a, 1998b) in Japan, most terrorist attacks in the later part of the twentieth century have used conventional weapons. The terrorists' favorite *modus operandi* is bombing, and this is likely to remain the primary instrument of terrorism because bombs are easily and inexpensively manufactured and simple to activate. Most publications in the medical literature deal with incidents of mass casualties caused by conventional explosive devices of various sophistication and power. In the past, most bomb explosions were the result of military conflicts, but at present, terror-related bombings predominate in addition to the continued existence of warfare and military engagements.

Improvements in prehospital trauma care and development of emergency medical service (EMS) systems resulted in improved response and shorter

evacuation time of patients to trauma centers. It also exposed the modern medical systems to a new challenge: the management of patients with severe blast injuries that previously would have succumbed to their injuries before transfer to medical facility. With this new challenge and the increase in numbers, severity, and magnitude of terror-related events, physicians will increasingly be involved in treating victims of mass casualty incidents, which will require a broadening of their existing skills and detailed knowledge of various mechanism of injuries. This knowledge will improve the level of care and outcome of patients with this specific and unique type of injury.

Detonation and Explosion

The explosive can be of military, commercial, or homemade origin, and it usually uses trinitrotoluene. Metal particles of various shapes often are added to the explosive to increase its wounding potential. Steel balls, nails, nuts, and the like are the most common. The explosive is detonated by an electrical charge activated remotely or through a switch operated by a suicide bomber. After detonation, a small portion of the energy is "wasted" on the rupture of the shell casing of the bomb, whereas the remainder of the energy transforms the solid explosive into gaseous form (Owen-Smith 1979), generating a highly pressurized wave of air that propagates radially from the site of explosion at the speed of sound followed by a wave of negative pressure. The leading front of this massive air movement is termed the *blast front*, and it is responsible for the peak of high pressure that will cause varying types of damage according to its intensity. A larger quantity of explosive will prolong the duration of the blast front, adding to its wounding potential. The propagation of the blast front depends on the density of air and the blast wind velocity. Higher velocities result in more severe injuries and a greater number of casualties. The metal additives energized by the blast and their injury potential is proportional to the size and nature of the explosive charge, their shape and weight, and the distance of travel.

Mechanisms of Injury

Explosion induces four classes of injury (Frykberg 2002):

- Primary blast injury, induced by the blast itself
- Secondary blast injury, caused by the projectiles

- Tertiary blast injury, caused by thrusting the victim against stationary objects and by wind disruption
- Quaternary injury, resulting from fire and heat generated by the explosion

Primary Blast Injuries

The blast wave itself causes the primary and tertiary injury patterns, and perforation of the eardrums and lung injury are the hallmarks of blast wave injury. When the blast shock wave travels from one medium to another of less density, such as tissue fluid to air, as happens in the lung alveoli, local tensions are created in the first medium (the spalling phenomena) and causes microscopic and macroscopic tears to the tissue at the interface. Following this insult, hemorrhage and edema develop in the lung or walls of the hollow viscus (Cooper 1996; Cooper et al. 1983). The blast forces exerted on the tissue are a stress wave, which causes damage according to its peak amplitude and shear wave, which relates to the peak's velocity and strain forces. Spalling and implosion are the putative mechanisms of blast tissue damage. The elastic properties of the tissues involved, their density and composition, determine the nature of injury, and consequently different damage is caused in different organs. The human body is remarkably resistant to the blast waves; solid or fluid-filled organs are rarely damaged whereas gas-containing organs suffer the most. Although the blast wave has little or no effect on fluid-filled and solid organs, their interaction with it may accelerate the blast wave's velocity beyond the speed of sound and increase the potential of injury from greater stress forces.

Secondary Blast Injuries

Secondary blast injuries are caused by projectiles embedded in the explosive, including the particles of the bomb's shell. This type of injury is common because the victim does not have to be close to the bomb to be injured. The velocities attained by these projectiles are sufficient to penetrate the body. Indeed different injury patterns have been defined for spherical missiles, nails, and screws. Such multiple penetrations to the body demand special awareness during evaluation, and all means of evaluation should be used to exclude cardiac or vascular injuries in these patients.

Tertiary Blast Injuries

The tertiary mechanism of injury involves displacement of the whole body by the blast. The blast wind can generate an acceleration of 15 Gs to a 75-kg

adult. The human body is relatively resistant to acceleration so injuries are mostly inflicted at the deceleration phase. At this phase tumbling or impact with rigid surfaces can result in multiple injuries, including closed head injuries and fractured bones (Cooper et al. 1983).

Quaternary Injuries

These injuries include flash burns, inhalation of toxic gas, and crush injuries caused by falling debris and collapsing buildings (Cooper et al. 1983; Frykberg & Tepas 1988). The flash produced by the detonation of the explosive can produce significant skin burns due to high temperature gases that can reach 3000 °C (Marshal 1977). This type of injury causes mainly superficial damage to exposed areas because clothing provides reasonable protection. Proximity to the detonation can cause severe third degree burns and fatality (Marshal 1977). The prevalence of burn injury among survivors of bomb explosion is controversial. Frykberg and Tepas (1988) reported that this type of injury is uncommon among survivors, and Stein & Hirshberg (1999) reported that 31% of the survivors suffered from burn injury. Other organs suffer true blast injuries as well. Head injuries cause some of the dead-on-scene events. The lucid interval of brain injuries is another manifestation of blast effects. Abrasions of the sclera and lens dislocations are rare, yet representative of blast injuries of the eyes.

Quinary Injuries of the Explosive

Sorkin et al. (2004) recently has described an apparent new pattern of blast injury that is termed the *quinary* injury pattern. In several victims of a recent Tel Aviv bombing, a hyperinflammatory state was observed without any other injuries that could explain it. Tachycardia, fever, low central venous pressure, and an excessive demand for fluids to maintain adequate tissue perfusion were noted in these victims. Considering the special explosive that was used, DETA—Sheet or pentaerythritoltetranitrate (PETN), which possesses vasodilatory properties—we have postulated that the bizarre hyperinflammatory state, unrelated to the severity of injury, resulted from absorption of this explosive.

CHARACTERISTICS OF THE PRIMARY BLAST INJURIES ON SPECIFIC ORGANS

Pulmonary Injuries

The overpressure that is needed to cause primary blast injury to the lung is approximately 40 psi (276 kPa). More than 50% of victims suffer pulmonary

damage with pressures of 80 psi (552 kPa) or more, and overpressures in the magnitude of 200 psi (1,379 kPa) or more are uniformly fatal unless protective measures are taken (Owen-Smith 1979). The greatest morbidity and mortality from the blast effect is due to the lung injury. Microhemorrhages appear in the alveoli, perivascular and peribronchial disruptions occur, and alveolar walls are torn leading to the development of blood-filled emphysematous lungs (Phillips 1986; Hadden et al. 1978). Some of these injuries present as simple or tension pneumothorax.

Alimentary Tract Injuries

Deceleration forces are the cause of injuries to solid organs, such as the liver, spleen, and kidney. One possible mechanism of genuine blast injury is the acceleration of organs from the blast wave and then deceleration due to their anatomic attachment. However, it is more likely that acceleration and deceleration of solid organs result from the tertiary blast mechanism, namely the bumping of the body against other objects, resembling classical injury of blunt trauma. In bombing, perforation of hollow abdominal viscera is uncommon (0–1.2%) and its incidence depends on the amount of explosive, proximity to the explosion, and enclosure of explosion site. Frank bowel perforation may be delayed for hours due to the special mechanism of its development. It was suggested that slow mucin dissection between the wall layers of the bowel could be the underlying mechanism of hollow viscous perforation (Cooper 1996).

We suggest that sometimes delayed bowel perforation is the result of mesentery tears or mesenteric avulsion leading to bowel wall ischemia and eventual perforation. We have treated several cases where mesenteric tears and avulsion about the terminal ileum and cecum were found, suggesting a mechanism of acceleration–deceleration in this type of injury. The greater amount of gas in the large bowel may be the reason why the small bowel is relatively spared. Injuries occur mainly in the cecum and colon, and others involve the ileocecal region (Paran et al. 1996).

Auditory System Injuries

Eardrum perforation occurs at very low peak overpressure, with 50% likelihood of eardrum perforation between 1.05–3.5 kg/cm^2 $\leq$15–50 psi (103–345 kPa), and therefore it is considered an indication of the patient's exposure to the blast. However, because cerumen-filled auditory canals and eardrums of younger victims are relatively resistant to the blast,

intact eardrums are not indicative of the exposure in these patients, and other signs of injury should be sought. The most common finding is a perforated eardrum in the anteroinferior part of the pars tensa (Pyper & Graham 1983).

LIMB AMPUTATION

In some patients, the dynamic pressure from the blast wind may result in limb amputation, and major limb amputation is a positive predictor for the severity of injury. Indeed, most of the injured suffering major limb amputations succumb to their injury in the field, while few will reach the hospital alive. Their severe injury pattern and the knowledge that amputation is a grave prognostic sign should not discourage teams from treating such patients in mass casualty events, since our experience has shown that most of them survive and eventually are discharged.

CAUSES OF IMMEDIATE DEATH

Massive pulmonary bleeding with suffocation and massive air embolism are causes of death by some reports (Marshal 1977); in one report, injury to the brain was the most common cause of death (Frykberg & Tepas 1988). Traumatic amputation is common among the immediate fatalities and occurred in 11% of fatalities from bombings (Marshal 1977). As many as 30% of the fatalities in cases of suicide bombing in Israel have had no obvious external cause of death (Stein & Hirshberg 1999).

FORENSIC STUDIES

Forensic studies provide information about the cause of death in terror bombings, especially for victims without distinctive injuries. In some of them the explosion caused cardiac dysrhythmia or air emboli that induced cardiac arrest and death, and such hidden injuries often are related to the impact of the blast. Because most victims that died on the scene suffered from the combination of blast, ballistic, and thermal effects of the explosion, the recognition of these differing death patterns and their correlation with the underlying mechanisms of injury could help to develop strategies for diagnostics and treatment.

SITE OF THE EXPLOSION AND THE WOUNDING POTENTIAL

In the civilian setting, sites of bombing have been classified as open, closed, or ultra-confined spaces. When the same explosion charge was detonated in closed quarters and not in open air, a distinctive increase in morbidity and mortality was identified (Mellor & Cooper 1989, 1992). In open air explosion, a rapidly expanding sphere of gas at high pressure travels from the center of the explosion, propagates through and around the objects in its path, and intensifies by the reflection of the shock wave from the ground to form the *machstem*. The quick dissipation and slowing of the shock front in open spaces leads to low immediate and late mortalities and to predominantly noncritical injuries. In confined spaces, the blast is bounced off the walls and consequently immediate and late mortalities and morbidities increase, and a higher incidence of blast lung occurs. In ultra-confined spaces like busses, the localized area of overpressure from the explosion is instantly amplified by repeated reflections from the enclosing walls, and therefore bus bombings are highly lethal.

THE MULTIDIMENSIONAL INJURY PATTERN

When different classes of injury occur simultaneously in the same patient, a multidimensional injury pattern (MIP) is recognized. In this subgroup of bombing patients the severity of injury is not adequately projected by the classic injury severity scoring (ISS) system, and therefore their diagnosis and management must differ from that of the conventional severe trauma patient. The multiple injuries in MIP challenge diagnosis, decision making, and treatment. These patients are more likely to require surgical intervention, to stay longer in intensive care and the hospital, and their in-hospital mortality is significantly above that of other patient groups, emphasizing the unique nature of this subgroup of bombing victims (as will be described later in the discussion). Because visceral injuries in bombing can occur from multiple wounding mechanisms, the conservative selective management that commonly is practiced in stable patients from conventional trauma must be applied cautiously, especially since delayed tissue breakdown in these injuries may result in missed injuries.

BLAST INJURIES: PREHOSPITAL MANAGEMENT

In the 1990s the reports about blast injuries came from Belfast, Ireland (Hadden et al. 1978; Pyper & Graham 1983; Mellor & Cooper 1989) or other sporadic reports from Beirut (Frykberg et al. 1989), Paris (Rignault & Deligney 1989), and Israel (Adler et al. 1983; Katz et al. 1989). We could not find any information about the roll of EMS in the management of those injuries. Since the outbreak of the blast explosions caused by suicide terrorist attacks in Israel in 1994, Israel became the main source for information and expertise for the medical management of victims of such events (Stein & Hirshberg 1999; Leibovici et al. 1996; Hiss & Kahana 1998; Pizov et al. 1999).

Magen David Adom (MDA)—the National EMS of the State of Israel—played a major role in the triage, treatment, and evacuation of the Israelis injured by those explosions. In 1995, the State of Israel took its first steps in establishing the national trauma system, and MDA had to determine the policy of prehospital treatments for trauma patients. The two options were "Scoop and Run" as in North America (Pepe & Steward1986; Cayten et al. 1993; McCallum & Rubes 1996; Cooke 1999; Royal College of Physicians and Surgeons 1999), or "Stay and Play" as in Europe (Schuttler et al. 1995; Schou 1996; Rossi 1997; Sefrin 1998). Magen David Adom Advanced Life Support (MDA's ALS) professional activities were based on the American doctrine, but we had physicians in most of our ALS teams, so we decided that our new trauma treatment policy will comprise the advantages of the two existing methods. The treatment will be according to the American Prehospital trauma life support (PHTLS) guidelines but with one modification—all the life-saving procedures must be completed on the scene prior to the evacuation, and the stabilizing procedures will be given *en route*. We called this method *Save and Run*.

In the last decade, MDA teams treated 50,000 trauma-injured patients per year according to the Save and Run guidelines. In the first *Intifada* (1994–1996), almost 1000 injured were managed by MDA teams in 20 explosions caused by suicide bombers, 11 of them defined as Multi Casualty Incidents (MCI). The data collection, a very thorough operational and medical debriefing, and the lessons learned from the prehospital management of those events, formed the basis for the new doctrine and updated protocols for MDA teams when the *Al-Aksa* (second) Intifada started in September 2000.

Guidelines for MDA Teams in Response to an MCI Situation

1. Fast recruitment of MDA teams and vehicles from the local and nearby regions. All the employees and volunteers are alerted by pagers. Some of the ambulances not on duty are taken by employees or volunteers to their homes and are activated immediately from their homes to those incidents. In this way more ambulances arrive to the scene as soon as possible.
2. The first paramedic to arrive at the scene takes command over the incident, reports to the dispatch center, divides the scene into sections, and establishes contact with the police, fire brigade, and military commanders on scene. Later, the paramedic is replaced by a senior managerial official from the region and joins the medical care providers.
3. Triage at the scene categorizes the casualties into three categories: urgent—red tag; not urgent—green tag; dead—black tag. This triage is carried out after primary assessment by advance life support (ALS) and basic life support (BLS) providers. The use of black tags and the decision not to treat those injured is done by ALS providers (doctors and paramedics) only.
4. Life-saving procedures including intubation, chest drainage, and control of massive hemorrhage are performed on the scene, using the Save and Run method. When ALS providers are not available in a section of the scene, the severely injured are loaded immediately into the ambulances and evacuated to the nearby hospital (Scoop and Run).
5. Secondary triage is performed by ALS providers (when not enough vehicles for evacuation arrive to the scene), who divide the injured into three categories: urgent unstable—red tag; urgent stable—yellow tag; not urgent—green tag. All victims are evacuated from the scene according to their category or color of their tag.
6. Dispersion of the injured: When more than one hospital is in the region, the dispatch center will instruct the teams on the scene to evacuate the same number of injured to each of the hospitals. The severely injured transported by BLS teams will always be evacuated to the nearest hospital.

7. Regulation of the injured: In a region where one of the hospitals is a Trauma Center Level 1, all the severely injured (especially head or chest injuries) will be evacuated to a Trauma Center.

In two instances the severely injured will not be evacuated to a Trauma Center:

a. The injured is evacuated at BLS level (Scoop and Run).
b. The injured has an immediate life-threatening injury and will not survive the trip to a distant Trauma Center.

All the hospitals in Israel are trained to respond to MCIs and treat the injured. Secondary triage of severely injured victims from general hospitals to Trauma Center level one is done by MDA ALS teams. For long distance interhospital transportation, helicopters are used. Since the outbreak of terrorist attacks in Israel during the *Al-Aksa Intifada* in September 2000 up to December 2005, 71 incidents of bomb explosion caused by suicidal terrorists attacks resulted in 2,769 casualties that were treated and evacuated by MDA teams. These terrorist suicide bombers attacks were characterized by three major differences from previous terror attacks:

- A vast number of attacks and casualties. There were two explosion in one day.
- All the explosions (except three) were detonated by suicide bombers.
- A new bomb composition—metal fragments: nails, bolts, and small balls were added to the explosives. Those shrapnel caused additional life-threatening injuries.

Of these incidents, 36 were defined as MCI, and 30 or more casualties were treated and evacuated by MDA teams per incident. The total number of casualties in the 36 incidents was 2,048 (an average of 57 casualty per event). Two hundred forty-seven (11.5%) were declared dead at the scene, and 410 (20%) were defined as urgent by MDA teams. The mortality rate (11.5%) changed according to the location of the explosion.

In buses the mortality rate is highest, at 15.9% (see Figure 10-1). In confined spaces the mortality rate is 13.5% (see Figure 10-2). In open space the mortality rate is 7.4% (see Figure 10-3).

MDA forces amassed the following in the 36 MCI (average values) (see Figure 10-4):

- **Ambulances**: 42 per event, range (24–57), 22% ALS vehicles
- **Team members**: 116 per event, range (75–198), 17% ALS providers
- **Time elapsed**: from explosion (average values):
  - **a.** Arrival of first ambulance: 3.9 minutes, range (1–14 min)
  - **b.** Evacuation of the first injured: 10.7 minutes, range (5–22 min)
  - **c.** Evacuation of the last urgent injured: 25.2 minutes, range (19–44 min)

FIGURE 10-1
Halissa bus bombing, Hifa. December 2, 2001.

The outcome and survival of casualties in critical condition at the scene of blast explosion depends on four factors related to prehospital management:

1. The primary triage procedure
2. Life saving treatment on scene
3. The evacuation system to hospitals (trauma centers versus regional hospitals)
4. The time elapsed from the explosion to definitive treatment in the hospital (the Golden Hour)

We chose these four criteria as nominators for the quality of the prehospital management of the victims of terror-related MCI in Israel.

FIGURE 10-2
Matza Resturant bombing, Haifa, March 31, 2002.

TRIAGE

The definition of urgent injury for MDA teams in MCI is "the delay in treatment and evacuation may threaten the life of the injured." Thus, 20% (410) of the 2,048 casualties were defined by MDA's teams as urgent. The urgent category includes three subgroups:

1. Dead on arrival (DOA): 10.2% of those injured who had vital signs in the early stage (few minutes

FIGURE 10-3
King George Street bombing, Jerusalem, March 21, 2002.

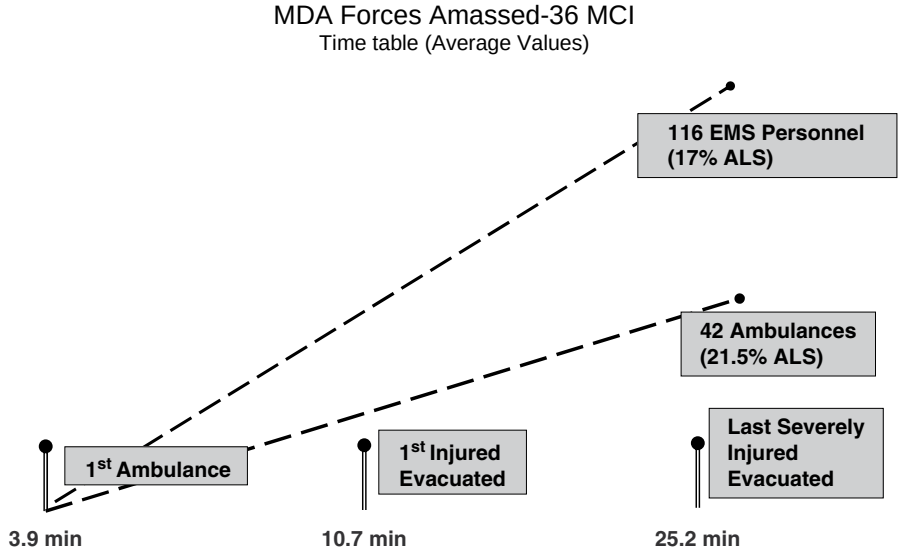
after the explosion) when the ALS providers reached the scene were treated, including the use of life-saving procedures, and were evacuated to the hospital but could not make it and were dead on arrival.

2. Severely injured casualties: 56% of those injured, with the severity according to the hospitals data international scoring system as (ISS) >16.
3. Less severe injuries: 33.8% with no immediate life-threatening injuries.

The less severe injuries, 33.8 %, includes injured with ISS 9–16, which are still urgent patients. Thus, the real *overtriage*, estimated to be 20%, is a reasonable estimate for prehospital triage in the chaotic situation of terror-related MCI (see Figure 10-5).

Metal fragments (nails, bolts, and small balls) added to the explosives caused unique and unreported clinical manifestation of injuries. Some casualties that were walking and conscious in the first hour after the explosion had small metal fragments in essential organs like the heart, liver, and brain. They were defined initially as not urgent by EMS and Emergency Department (ED) personnel. Only X-ray or late deterioration in the hospital revealed their life-threatening injury. We estimate

FIGURE 10-4
Response of the National Emergency Service of the State of Israel (MDA) to a multicasualty Incident (MCI).



this *undertriage* number to be 1% to 3% of the not urgent casualties (n = 15–45).

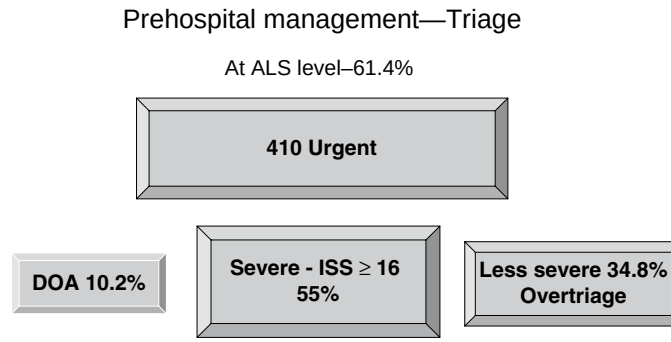


FIGURE 10-5
Pre-hospital management of triage for advance life support (ALS).

Life-Saving Procedures Performed at the Scene by MDA's ALS Teams

According to the Save and Run method, most of the life-saving procedures completed at the scene included 99 life-saving procedures:

- Intubation: 69 successful
- Chest decompression: 15, most by needle
- Massive hemorrhage control: 15, with tourniquet, pressure dressing, or finger pressure

Of those,

- Survival to hospital: 66
- 226 severely injured ISS ≥ 16
- Life saving procedures: 43.8%

One third (n = 33) of those life-saving procedures were performed on unsalvageable casualties and they arrived dead to hospitals. Of those critically injured, 66 survived the trip to the hospital; 59 of them survived to discharge from the hospitals. Twenty-six percent of all the severely injured casualties (n = 266) survived to discharge from the hospital as a result of the life-saving treatment provided by MDA's ALS teams at the scene.

Evacuation of MCI Casualties to Various Hospitals

Trauma centers versus regional hospitals:

- Evacuation to hospitals: at ALS level 42%
- Region A: No Level-1 TC {9}
  - 49 severely injured evacuated
  - 63% of them secondary transferred to TC-1 {9}
- Region B: Level 1-TC {27}
  - 90 {71%} severely injured evacuated to trauma center
  - 37 {29%} severely injured evacuated to general hospitals
  - 12% secondary transferred to Level-1 TC

For MCI in peripheral and small town regions (12 events), there was no Level-1 trauma center within reasonable distance for primary evacuation. All 82 severely injured were evacuated to regional hospitals; 42% were transferred secondarily by MDA's ALS teams to trauma centers from distant regional hospitals by helicopter.

For MCI in central city regions (24 events), there was at least one Level-1 trauma center in the region. In 11 MCI, the trauma center was the nearest hospital to the site of the explosion:

- 170 severely injured were evacuated to hospitals
- 125 (74%) were evacuated primarily to a Level-1 trauma center
- 45 (26%) were evacuated to regional hospitals
- Only 12% were transferred secondarily to trauma centers

The time elapsed from the explosion to definitive treatment in a hospital (the Golden Hour) was as follows:

- Evacuation of the last urgently injured (average value for 36 MCI) was 25.2 minutes, range: 19–44 minutes
- Transportation was less then 15 minutes, range: 4–26 minutes
- Time elapse from explosion to arrival to the hospital—Average value: 40.2 minutes
- Time elapse from explosion to arrival to the hospital, range: 23–70 minutes

Most of the urgent injured arrived to the hospital in the time range of the Golden Hour.

TRIAGE AND CONTROL IN A LEVEL 1 TRAUMA CENTER

The sudden surge in the inflow of victims following a bombing attack presents medical and logistical challenges to physicians, medical, paramedical, and hospital administration. The logistical challenge is to rapidly process a large number of casualties through the system, and the medical challenge is to provide the best possible trauma care to all victims (Hirshberg 2004). Medical and administrative concerns such as ambulance arrival, triage of victims at the entrance to the hospital, control of event proceedings, and resource management need to be addressed and modified to improve delivery of care for in-hospital triage.

Frykberg (2002) reviewed several terrorist bombing events and has shown that overtriage correlated with critical mortality (r = 0.92). The mean overtriage rate in those attacks was 59%, similar to more recent publications from Israel (Trauma Division Report 1997). Hirshberg used a computer model to show that overtriage rates of 50 to 75%, which are routinely practiced in civilian trauma, shift the sigmoid-shaped graph to the left, thus decreasing the surge capacity (see later). Undertriage, which is detrimental in any trauma scenario, is obviously more so during bombing attacks. This is due to the fact that the most experienced trauma surgeons will be assigned to a trauma unit setting and the remaining victims will be directed to lower levels of care. It is vital to weed out the victims who will do well with minimal care and those who will die despite maximal care, and focus on those who will benefit the most from optimal trauma care and rapid surgical intervention (Hirshberg et al. 2001). Thus, the process of triage, which tries to match the injury with the appropriate level of care, is probably the most important decision-making point during a bombing attack and should be performed by the most experienced trauma surgeon.

From the trauma care perspective, a small number of critical victims requiring urgent care are immersed within a larger group of less severe casualties who can tolerate some degree of suboptimal care, the so-called "minimal acceptable care" (Stein & Hirshberg 1999). Data from the Level-1 trauma center at Hadassah University Hospital (HUH) show that as many as 18 victims were brought to the ED within six minutes, eight (44.4%) were admitted for more than 24 hours, and four (22.2%) severely injured victims were admitted to an intensive care unit (ICU) (Almogy et al. 2006).

In victims of suicide bombing attacks, who suffer from a multidimensional injury pattern, the severity of injury cannot be assessed using classic injury scoring systems (Kluger et al. 2004). Almogy and Nelson have shown that the presence of certain external signs of trauma is associated with more severe injury. Signs such as limb amputations, burns, open fractures, and multiple long bone fractures are associated with an extremely high fatality rate at the scene (Almogy et al. 2005; Nelson et al. 2006). The authors have shown that penetrating head wounds odd ratio (OR) (OR 3.47) and injuries to four or more body regions (OR 4.12) are predictors of blast lung injury (BLI), and penetrating torso wounds (OR 22.27) and injuries to four or more body regions (OR 4.89) are predictors of intra-abdominal injury requiring laparotomy (Stein & Hirshberg 1999).

Control

Control and coordination are achieved by the "accordion approach," in which patient evaluation and management proceed through repeated cycles consisting of a dispersal and a convergence phase (Almogy et al. 2004). The most experienced trauma surgeon is appointed surgeon-in-charge (SIC). Activity is coordinated and controlled by the SIC, who is aware of the overall situation and has the oversight to prioritize evaluation and treatment. The SIC does not take an active part in patient care; rather he or she is responsible for:

1. Performing triage at the entrance to the ED and directing the victims to the appropriate level of care.
2. Determining preferences for utilization of limited resources such as operating rooms, admissions to the ICU, and computed tomography (CT) and angiographic studies.

The SIC repeatedly examines and evaluates the victims with the treating teams. The SIC, typically the Chairman of Surgery, is in continuous contact with the ICU attending-in-chief, the Chairman of Anesthesia, and chairpersons from other departments. Chaos gradually is managed once the number of patients requiring further work-up is reduced. The overall condition of the patient, the sequence of therapy, the need for further imaging studies, and the need for ICU admission are discussed and finalized.

In analyzing this approach we must consider the following:

- Many hours and sometimes days are required for the situation to stabilize and eventually normalize.
- Treating teams are physically and emotionally exhausted.
- Repeated reassessment by the treating teams and SIC to ascertain that all victims receive optimal care is fundamental.

In these circumstances, a strong personal commitment by the treating teams and hospital administration are pivotal to success. Depending on the magnitude of the attack, this commitment may last from several hours to several days.

Victims who require control of bleeding and those with life-threatening injuries such as chest, abdominal, and head injuries are the first to undergo surgery. Victims with limb-threatening injuries such as long bone fractures

and extensive soft tissue damage comprise the majority of patients who require surgery within the first 24 hours (Shamir et al. 2004). They will be taken to the OR once their imaging studies are completed, and an adequate number of operating rooms and ICU beds have been made available.

Initial Evaluation

The majority of victims of penetrating trauma sustain injuries to isolated parts of the body such as the head, chest, abdomen, or limbs. Blunt trauma is more commonly a multisite injury, the severity of which depends on the mechanism of injury. The injuries sustained by victims of suicide bombing attacks share the worst of both worlds. The multitude of heavy particles causes damage to a large surface area, much like blunt trauma. Each particle causes extensive tissue damage at the site of entry, much like penetrating trauma. Survivors typically suffer a combination of wounds of varying severity and location and the diagnostic work up is focused on determining the extent of damage caused by each missile (Aharonson-Daniel et al. 2006).

Attention is given to the presence of blast injury, and the tissue damage inflicted by penetrating missiles. A liberal approach to imaging studies is preferred and the work-up is tailored to the injuries, and not to the situation. Thus, bedside sonograms and the necessary plain films are performed for each and every multiple injury victim. CT scan and angiography are extensively performed for victims of terrorist bombings (75 and 11%, respectively) (Almogy & Rivkind 2006).

Intensive Care Unit

In a review of the experience at HUH following 14 terrorist bombings, Shamir et al. found that the ICU received an average of four victims/attack, and that 86% were mechanically ventilated. Victims stayed in the ICU for an average of 4.5 days, considerably longer than the entire ICU population (Aschkenasy-Steuer et al. 2005; Shamir et al. 2004). Mean time to first ICU admission was five hours, depending on whether the victims were transferred from the ED and angiography suites (3.8 and 3.7 hours, respectively) or the OR (6.3 hours). Only two of 108 patients (1.9%) were admitted to the ICU within one hour. Two conclusions emerge from examining this data: (1) the ICU's intrinsic capacity cannot handle the number of victims, and (2) additional ICU beds are required only three hours from the event. These problems have been handled by

transforming PACU beds into fully-equipped and staffed ICU beds, and by reviewing the condition of all ICU patients to determine which are suitable for transfer.

Resources and Administration

Hirshberg et al. (2005) developed a computer-simulated model to analyze the inflow of patients during MCI and attempt to define the parameters that influence the success of treatment. The model predicts a sigmoid-shaped curve for the level of care as a function of the critical casualty load. The surge capacity was represented by the upper flat portion of the graph; the slope represents the point where the trauma system begins to fail, and the lower flat portion the point where the trauma system is no longer providing care. The authors demonstrated that by recruiting maximal personnel and resources, the sigmoid-shaped graph can be shifted to the right, increasing the surge capacity from 4.6 to 7.1 critical patients per hour.

Following bombing attacks, the number of victims requiring surgery and the median number of operations is high, as is the number of different teams involved in treatment. Data from Israel show that over half of hospitalized victims of bombing attacks required surgery within eight hours of admission and 23 to 49% were admitted to an ICU (Aschkenasy-Steuer et al. 2005). Four hours following the attack, an average of three operating rooms were taken up by victims, in addition to ongoing surgery, and as many as seven operating rooms were in service simultaneously on victims of the attack. This heavy workload, which can continue for eight hours and longer, demands all available personnel.

Major and minor changes to resource management must be made to cope with these challenging situations. OR schedules need to be adapted to the developing situation; that is, overcrowded ICUs and exhausted teams; postponed elective radiology studies; and nonurgent tasks such as academic, research, teaching, and outpatient clinics, as well as personal commitments must be temporarily sacrificed.

THE EPIDEMIOLOGY OF TRAUMA CASUALTIES

Recent years brought about an upsurge in terrorist activities worldwide. Israel has been exposed to sporadic periods of terrorist activities for decades, with a noteworthy increase since September 29, 2000. By the end of 2003, 6,049 persons have been injured and over 904 killed

due to terrorist acts in the country (IDF 2004). Many of these attacks are explosions of suicide bombers resulting in mass casualty events. Mass casualty events are incidents in which the medical system is overwhelmed and the balance between resources and demands is destabilized (Shapira & Shemer 2002). These latest terror attacks were characterized by a new bomb makeup—bombs that contain metal particles of various shapes that increase their wounding potential (Kluger et al. 2004; Stein & Hirshberg 2003). The consequences are more severe injuries than encountered before, bringing up the possible need for updating protocols for evacuation, triage, and hospital preparedness (Almogy et al. 2004; Michaelson et al. 2003). Furthermore, since injuries were different from previously encountered trauma, the pattern of demand for resources, and the medical proficiency necessary for treating new terror victims, were different than before (Adler et al. 1983; Michaelson et al. 2003; Einav et al. 2004; Peleg et al. 2003a, 2003b; Lynn et al. 1999; Hiss et al. 2002; Emile & Hashmonai 1998). Additionally, as mass casualty incidents became a frequent event, the need to maintain continuous preparedness of emergency care services and trauma centers in the country in order to cope with them increases.

As we strive for better preparedness of hospitals and physicians to treat terror casualties, we tried to learn as much as possible about the characteristics and epidemiology of this new "disease."

Methods

Data on trauma-related hospital admissions are recorded routinely in the Israeli National Trauma Registry. This data, for the period between September 29, 2000 and December 31, 2003, was retrieved, reviewed, and analyzed. Patients included in the registry are all trauma-related hospital admissions at 10 hospitals, including all six Level-1 trauma centers in the country. Transferred patients and those who died in the emergency department are included as well; patients who were declared dead on arrival or those who died on the scene are excluded. Data includes demographic information, injury diagnosis detail and severity indicators, treatments provided, hospital services utilization, and outcomes. Terror-related injuries were identified and selected as the study population. SAS software was used for statistical analysis, which included Chi square tests, Wilcoxon sum of rank tests, t-tests, and a logistic regression analysis to determine risk factors for inpatient mortality.

Results

A total of 1,789 patients were hospitalized at the 10 hospitals that took a part in the Israel National Trauma Registry between September 29, 2000 and December 31, 2003 due to injuries inflicted by terrorist acts (ICD-9-CM external cause of injury code E990-E998). Males comprised 73.4% (n = 1313) of the casualties. More than half of the terror casualties (54.8%) were young people, aged 15 to 29 years. This differs significantly from the age distribution of patients with other trauma that are usually either younger (29.9% aged 0–14 years) or older (24% above 60 years old). The age distribution of casualties is presented in Table 10-1.

Terror casualties suffered a much higher proportion of severe and critical injuries than other trauma types (27.4% versus 10%). This also is reflected in the hospitalization rate—normally, one in 10 emergency room attendees would be admitted; in terror mass casualty incidents, one in three are admitted. 6.3% arrived to the emergency department in shock, with systolic blood pressure below 90 mm Hg, more than double the rate found in other trauma. They subsequently consumed more hospital resources

Table 10-1 Characteristics of Terror Casualties Compared to Nonterror Casualties

	Terror		Nonterror	
	N	%	N	%
Total	1789		69877	
Males	1313	73.4	42854	63.0
Age (y)				
0–14	128	7.3	20236	29.9
15–29	965	54.8	15061	22.2
30–44	368	20.9	9412	13.9
45–59	182	10.3	6770	10.0
≥60	118	6.7	16217	24.0
Severe Injury (ISS 16–24)	189	10.8	4063	6.0
Critical Injury (ISS ≥25)	292	16.7	2738	4.0
Systolic BP <90	108	6.3	1655	2.6
Surgery	302	49.8	9099	38.4
Intensive care unit (% stay)	443	24.8	4756	7.0
Total LOS > 14 days	336	19.0	5693	8.4
Inpatient Mortality				
In severe/critical (ISS 16+) patients	108	22.7	901	13.4
In all patients	114	6.4	1296	1.9

All differences between the populations noted in this table were significant at P <0001.

and had worse outcomes, as can be seen in Table 10-1. Half (49.8%) of terror victims had undergone surgical procedures in the operating room, most of them in the first few hours of attendance. A quarter (24.8%) of the patients had been to the intensive care unit during their hospital stay. This is more than three times higher than in other trauma patients, where only 7.0% required intensive care unit care. The overall inpatient stay of terror patients was longer, with 19% of terror victims staying longer than 14 days compared to only 8.4% in nonterror patients. Median duration of stay was five days (interquartile range 2–11 days) in terror patients and three days (interquartile range 1–7 days) in other trauma. Crude inpatient death rate was 6.4% of terror victims compared to only 1.9% in other trauma. All these differences were statistically significant. When controlling for severity (looking at severe casualties only), and adjusting for age and sex, terror still increased the risk for dying by 2.3 (confidence interval 1.8–2.9). The majority of terror casualties, 976 (54.6%), were injured by explosion. These injuries are described in detail in other papers (Paran et al. 1996; Sorkin et al. 2004). Additional mechanisms of injury included mostly gunshot wounds (n = 671, 37.5%) and other mechanisms such as stabbings, intentional running over by vehicles, and stone throwing (total n = 142, 7.9%).

One of the important characteristics of explosion terror incidents is that they are mass casualty events—they affect a large number of people who are injured and killed simultaneously, and a very high percentage of them sustain multiple injuries, a fact that distinguishes them from the typical patient. Nearly 20% (n = 182, 19.2%) of explosion victims hospitalized suffered critical (ISS ≥25) injuries. Another 11.1% (n = 105) sustained severe (ISS 16–24) injuries. These proportions are significantly higher than in other trauma types (6% and 4%, respectively).

A significantly higher proportion of explosion victims had a computed tomography (CT) in the emergency department (37.2% versus 24.0%).

DISCUSSION

Terror mass casualty incidents are not similar to previously encountered mass disasters; terror injuries include blast injury, gunshot wounds, crush, and other severe conditions that occur in an inconsistent pattern of frequency. Terror mass casualty incidents are different from other

known disasters in their epidemiology—unique distributions of age, gender, mechanism, injury types, and so on (Peleg et al. 2003a, 2003b). Terror injuries presented the trauma system with new demands for preparedness and medical care.

The trend of suicide bombers has been on the rise in past decades. Suicide bombers choose the time and place of explosion, that together with new bomb compositions created new injury profiles that present a greater challenge to the health care system (Kluger et al. 2004; Almogy et al. 2004; Michaelson et al. 2003). These injuries cause multiple penetrating injuries (Kluger et al. 2004; Hirshberg et al. 1999) in addition to known effects of explosions such as burns, displacement by mass movement of air, and impact against rigid objects (Phillips 1986; Cooper et al. 1983; Katz et al. 1989).

The high rate of critical injuries presented and the frequent injury to multiple body regions means that a large proportion of the patients are in need of immediate care. Providing immediate care for a large number of severely injured patients is a challenge, and bottlenecks are prone to occur (Hirshberg 2004)—at the imaging facilities, at the operations theater, and possibly in the ICU. Trauma registry data demonstrated that imaging procedures, treatment in the emergency department, and first destination from the emergency department are significantly different in terror explosion mass casualty events than in other trauma, thus the staffing and organization should be adjusted accordingly to prevent bottlenecks from occurring and maintaining the ability to provide optimal care (Michaelson et al. 2003). Although children were injured, these were mostly youth (aged 15–17) (Aharonson-Daniel et al. 2003; Waisman et al. 2003), thus usually they were treated by general surgeons and hospitalized in the general wards.

CONCLUSION

New bomb composition changed patterns of injury type and injury severity in casualties of terrorism against a civil population. Casualties are younger, their injuries are more severe, and they involve multiple body regions and systems. Explosion casualties present in masses and use more hospital resources than other injury types. The severe form of injury of these patients presents a challenge for physicians and creates bottlenecks that are

better prevented by planning ahead and optimizing evacuation and triage procedures. Heavy use of hospital resources will also have cost implications. We hope that health care providers from around the world can use the information presented here to recognize what can be expected in such terror mass casualty incidents and prepare their health systems accordingly.

SUMMARY

The multidimensional, multifaced medical problems of taking care of blast and penetrating metal object injuries have put the vision of saving lives into a new perspective. The whole system of the continuum of care at its most comprehensive understanding had to revise its concepts and collaboration strategies. New medical, administrative, logistic, and paramedical challenges appeared and demanded quick implementation of the new knowledge and adaptation of new strategies. This information should also be taught to military medical systems on the battleground. Several issues still deserve a closer look:

- The injuries to the extreme population: infants, children, and geriatrics
- Newer type of ventilation on the scene
- Using nonconventional elements in the bomb
- Knowledge management of the information gathered

No doubt that such challenges bring closer the different members of the medical system, creating a pool of motivation, capabilities, and sharing knowledge.

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CHAPTER 11

The Soviet Experience in Afghanistan 1980–1989: Abdominal Blast Injury Produced by Mine Explosions

Petr G. Alisov

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INTRODUCTION: LAND MINES IN THE SOVIET–AFGHAN WAR

Mine warfare played an important role in the Soviet–Afghan military war between 1980 and 1989 (Antonov 1997). They were used mostly by the

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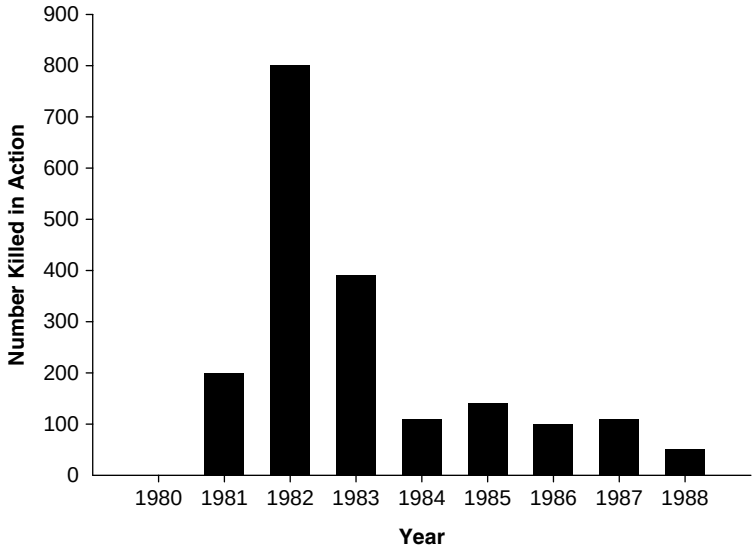
Soviet Army. However, the Afghan guerrilla fighters (the *Mujahideen*) used mines too, but to a limited extent. Initially they were more effective causing high death rates until effective mine countermeasures were developed by the Soviet Engineering Regimen that succeeded in reducing the losses significantly (Antonov 1997). These countermeasures included issuing personal protective flak jackets, sandbagging and reinforcing vehicle floors, and riding on the tops of the armored vehicles. Soviet personnel death peaked in the early years from 1981–1983 and then dropped. Vehicle losses peaked from 1984 to 1985 during the heaviest fighting period of the war, and then dropped markedly also (Lyakhovskiy 1995) (see Figure 11-1).

The number of Soviet personnel who served in Afghanistan is estimated to be approximately 620,000, of which about 53,753 (8.67%) were wounded or injured (Krivosheev 1993). Soviet soldiers wounded by shrapnel were 2.5 times those wounded by bullets. The proportion of multiple and combination wounds increased four times over the course of the war, and the number of serious and critical wounds increased two times (see Table 11-1). The primary cause for this increase in serious and critical injury was land mines. The number of wounded from land mines increased 25 to 30% over the course of the war (Nechaev et al. 1991). However, improved Soviet medical evacuation during the war allowed for greater survival of the critically wounded (Chizh & Makarov 1993). Throughout the course of the war, it is estimated that land mines caused 30 to 40% of the trauma cases treated by Soviet medical personnel (Yanov et al. 1997).

FIGURE 11-1

Soviet casualties in the Soviet–Afghan military war from 1980 to 1988.



In general, land mines include antipersonnel, antitank, and antivehicle devices. The mines can be detonated by pressure, sound, trip-wire, and remote control. Some mines are buried, placed on or above ground, and others spring out of the ground to explode at waist-level. The damage from mines can be through the blast effect of the explosive charge or from the fragments driven by the explosion. Mine injuries are caused

Table 11-1 Frequency of Wounds by Type and Severity as Proportion of Total Hostile Fire and Land Mine Wounds from 1980–1989 during the Soviet–Afghan War

Wound Type	1980	1981	1982	1983	1984	1985	1986	1987	1988
Bullets	62.2	54.7	50.4	46.0	34.1	36.6	31.8	26.5	28.1
Shrapnel	37.2	45.3	49.6	54.0	65.9	63.4	68.2	73.5	71.9
Multiple and Combination	16.0	21.1	29.5	47.6	65.4	72.8	68.8	65.8	59.4
Serious and Critical	23.1	27.7	31.1	47.1	52.4	51.4	50.2	50.1	45.2

primarily by blast or by shrapnel following detonation. Mines can kill those who directly trigger them or wound those nearby at varied distances depending on the mine charge. For those who step directly on a mine, the most common injury is the loss of a lower leg, with possible additional damage to the contralateral leg (Fomin 1994). Exposure to mine explosions produce polytraumatic injuries comprised of (1) limb fractures and/or amputation, (2) lacerations and wounds from secondary and tertiary blast effects, (3) cardiopulmonary contusion, (4) neurogenic and hemorrhagic shock, and (5) thermal burns, which are often complicated by infections (see Table 11-2).

During the war in Afghanistan, 86.5% of Soviet mine-casualties experienced shock, and it was observed that 10 to 15% of the casualties will probably go into a shock characterized by tachycardia, hypotonia, and cardiac dysrhythmias so severe that it is irreversible even with standard resuscitation of fluids and support, and blood pressure may fall well below

Table 11-2 Frequency of Complex Injuries Involving Different Anatomical Regions in Penetrated Abdominal Wounds (PAW) and Mine Blast Trauma (MBT) during the Soviet–Afghan War

Anatomical Region	PAW (%)	MBT (%)
Head	8.6	55.7
Neck	2.0	4.3
Chest	37.1	35.9
Spine	9.2	9.3
Pelvis	20.3	27.6
Extremities	35.7	58.8

tolerated level. Typically, the casualties will lose large amounts of blood. For example, 32.6% of Soviet mine casualties required 1 to 1.5 liters of blood, 53.1% required up to 2 liters, and 14.3% required up to 3.5 liters. As blood pressure dropped precipitously, massive forced infusion–transfusion therapy is necessary, but often fails. Surgical intervention such as amputations and other surgical care of the wounds within two or three hours of the infusion–transfusion therapy was poorly tolerated and frequently ended in death (Yanov et al. 1997).

MINE EXPLOSION AND THE HEART

Clinical diagnosis and electrocardiograms (ECG) showed that heart injuries further complicated treatment of mine injuries by causing myocardial ischemia, resulting in life-threatening dysrhythmias. It was found in autopsies that 45.6% of the mine casualties who died in the hospital had sustained some form of heart injury. These injuries were classified as focal, endocardial, and intramural hemorrhaging injuries, and ranged from a low to high blood flow from a damaged heart ventricle. Histological examination of the injured hearts revealed that the heart muscle fibers had no observable transverse striations and that they were missing nuclei and had distorted contours (Bisenkov & Tynyakkin 1992). Heart injury usually required a longer preoperative period than normal. The Soviet therapy regime involved administration of cardiac glycosides, steroidal hormones, and nonnarcotic analgesics. Treatment would also include administration of antiplatelet aggregation drugs and load reducers such as dipyridamole to reduce the risk of blood clots as well as antispasmodic drugs to relax the smooth muscles of the gut to prevent or relieve painful cramping spasms in the intestines. Myocardial metabolism was normalized by administering preparations of potassium, cocarboxylase including thiamine pyrophosphate (TPP) and thiamine diphosphate (TDP), adenosine triphosphate (ATP), and vitamins B and C. Once bleeding was stopped, the infusion–transfusion therapy would be reduced to limited amounts of fluids—mainly glucose-insulin mixtures and glucose-vitamin cocktails. All blood used for transfusions, particularly preserved blood, was thoroughly filtered (Bisenov & Tynyakkin 1992). The Soviet experience with mine casualties demonstrated also that typical time frames for surgical treatment of injuries did not apply in these cases. It was essential first to improve the contractile ability of the myocardium, eliminate

any electrical instability of the heart, and normalize the hemodynamic parameters before surgery took place (Bisenov & Tynyakkin 1992).

MINE EXPLOSION AND THE LUNG

Mines also caused extensive lung injuries and the casualties experienced profound traumatic shock. The primary symptoms of mine-induced lung injury included labored breathing, shortness of breath, tachycardia, marked drop in blood pressure, and cyanosis of the skin. It was observed that lung injuries, particularly if improperly treated, often resulted in death. Some 20 to 25% of Soviet mine casualties who sustained injured lungs developed focal pneumonia within the first hours of injury consistent with adult respiratory distress syndrome (ARDS). Autopsy of mine casualties revealed that 22.8% of lung injuries were characterized with large areas of blood-saturated tissue, and low-focal hemorrhage were noted throughout the lungs (Bisenov & Tynyakkin 1992).

MINE EXPLOSION AND THE CENTRAL NERVOUS SYSTEM

Land-mine casualties often suffered from a disturbance of the central nervous system, particularly those who have not had proper intermediate care. The Soviet clinical picture showed that these casualties would be brought into the hospital initially displaying symptoms of marked traumatic shock. The subjects would remain conscious and oriented during the first hours. Neurological examinations and a spinal tap would not show evidence of serious brain injury. However, attempts to regulate the hemodynamic indicators and breathing of the injured were generally not successful and the brain functions would begin to worsen, and the subject would lose consciousness or lapse into a deep coma. As a result, a significant number of the casualties would die from severe disturbances to the central nervous system. In general, Soviet preoperative procedures for land-mine casualties with brain damage took one to two hours and involved dehydration therapy beside paralysis and ventilatory support. Autopsies would show an ischemic softening of brain tissue with hemosaturation. It was found that if infusion–transfusion therapy did not normalize the hemodynamic endpoints in mine injuries, this was an indication that the subject had suffered heart injury, serious brain injury, or was in early

septic shock, and the Soviet medical personnel learned to adjust their treatment accordingly (Bisenov & Tynyakkin 1992).

MINE EXPLOSION AND SEPTIC SHOCK

Land-mine casualties are very susceptible to septic shock resulting from extensive tissue damage and progressive wound infection. In severe septic shock, it is very difficult to stabilize the hemodynamic endpoints since the vascular channels do not respond to infusion therapy and the myocardium undergoes a marked depression. The Soviet intensive therapy for septic shock involved administration of cardiac glycosides, large doses of steroids and enzyme inhibitors, antibiotics, low molecular weight, and rheologically active infusion substances in addition to freshly heparinized blood. Once the hemodynamic indicators became stable, it was very important to prevent pulmonary edema by careful use of diuretics (Bisenov & Tynyakkin 1992).

MINE EXPLOSION AND ORGANS OF THE ABDOMINAL CAVITY

Under these complex conditions, abdominal mine blast injury (AMBI) is overshadowed by the other more immediately life-threatening effects, which makes it difficult to diagnose and more often underestimated. It has been suggested recently that AMBI may cause lethal outcomes at a late phase, and therefore, requires surgical interventions. Considering that AMBI may determine the morbidity of these casualties that survive the first hour postexposure, a precise early diagnosis is essential to implement correct intervention. However, the pathogenesis of AMBI is poorly described in the medical literature and requires a further detailed analysis. The current report is based on analysis of 2,687 randomly selected medical records of abdominal injuries during the military operations of the Soviet Armed Forces in Afghanistan between 1980 and 1989. It is focused on epidemiology, pathogenesis, and the results of the conducted AMBI surgeries. Assessment of these 2,687 cases revealed that 11.1% were related to mine explosions, of which only 3.6% were diagnosed as AMBI (i.e., were not complicated by penetrating wounds to the abdominal cavity, etc.). Thus, this analysis is based on 97 cases of AMBI and is considered to be statistically significant for further development of recommendations for

Table 11-3 Frequency of Shock Levels among the Wounded with Penetrated Abdominal Wounds (PAW) and Mine Blast Trauma (MBT) during the Soviet–Afghan War

Shock Level	PAW (%)	MBT (%)
0	17.8	19.3
I	6.6	4.5
II	23.3	21.6
III	30.7	21.6
Terminal Stage	21.6	33.0

managements of AMBI. Frequency of damage to the different abdominal organs from land mine explosion is shown in Table 11-3.

It is much more difficult to diagnose victims of a mine-blast trauma with damaged organs in the abdominal cavity. What distinguishes them from those with other mine-blast wounds of the abdomen is the absence of damage to the integuments in the abdominal area. Mine-induced damage to the abdomen can be described according to whether it causes tearing of the extremities or not. Thus, if it affects the extremities, it is described as a mine-blast wound for extremity, and if its effects are limited to the abdomen too, it is described as a mine-blast trauma of abdomen. Usually mine-blast trauma of organs in the abdominal cavity is observed during demining due to the direct impact of incident energy from the explosion on the body.

The 97 case records of mine-blast trauma victims that sustained injury to organs of the abdominal cavity (3.6% of all abdominal wounds) were analyzed. It was observed that lethality from mine-blast trauma was 40.2%, with 78.4% having damage to multiple organs, and in 89.7% the abdominal injury was combined with injuries in other areas of the body. Damage of only one anatomic area was observed in 10.3%, two in 26.8%, three in 39.2%, four in 17.5%, and five in 6.2% of the cases.

Tearing off segments of extremities occurred in 8.2% of the victims. The extent of intraabdominal damage in the majority of victims was more than the damage to all other anatomic areas; however, in 16.5% of cases it was equivalent to the damage of other areas, and in 3.1% of the cases the damage of other areas of the body exceeded the extent of abdominal damage. Five injured (5.2%) during treatment after one to nine days have

been diagnosed with concomitant infectious diseases including hepatitis, malaria, and dysentery. At laparotomy, internal organs damage was not revealed in 10.4% of the cases, damage to one organ was revealed in 46.9%; two in 22.9%; three in 11.5%; four in 7.3%; and seven in 1% of the cases. More often (79.4%), the damage of parenchymatous organs was observed compared to hollow organs (34%). This was possibly due to the fact that parenchymatous organs possess greater inertia.

Spleen Injury

The spleen was more often the most vulnerable organ to damage in 54.2%. Its full destruction was revealed in more than half of cases and damage limited only to its capsules in 7.7% of the cases. In almost 90% of the cases sustaining spleen damage had a spleenectomy executed, and suturing of spleen wounds was done in 10% of the cases. Implantation of pieces of spleen tissue in the large omentum was made in 11% of cases undergoing spleenectomy.

Liver Injury

Liver damage was found in 37.5% of victims. However, the damage was asymmetrical. Thus, the right lobe was damaged four times more often than the left lobe, and the area of the liver gate was damaged even less often. In one case, extensive damage of the liver was combined with wounds to the portal vein and inferior vena cava leading to a lethal outcome. Superficial linear breaks were found more often, and deep cracks of hepatic parenchyma were found in 14.3% of the victims. In one case only, the resection of a liver was made. Suturing was made with tamponade of the liver wounds by haemostatic gauze, and was executed in two victims, and unloading holecystostomy also in two victims. Drainage of the underliver space was done in half of the victims with damaged liver.

Kidney Injury

Kidney damage was observed in 11.5% of the victims, in which the right kidney was damaged twice as often as the left kidney. Destruction of the kidneys was observed in 20%. Nephrectomy was executed in half of those with damaged kidneys and suturing of kidney wounds in 30%. The pancreas was damaged in 10.3% of the victims with its tail damaged more often. Parenchyma of pancreas suffered more often than the capsule. Suturing of the capsules was done in 30%, and insertion of parenchyma in 40% of the victims.

Stomach and Gastrointestinal Injury

The stomach was damaged in 4.1% of the victims, and its body was damaged more often. In only one case, the stomach wall was ruptured fully, and in three others, bruises of its wall with damage of a serous environment was found. The broken-off stomach wall was sutured, as well as the damaged serous environment. Bruised duodenum was revealed only in one case, and surgical intervention was not carried out. Small intestines were damaged in 20.6% of the victims. The intestinal wall was bruised and the serous environment was damaged in 80%, and full breaks in 20% of the cases. Full break of the intestinal tube was found in two victims. The damages occurred with equal frequency in both proximal and distal parts. Suturing of nonpenetrating wounds and subserous hematomas of the small intestine was made in nine victims, suturing of its wounds in two and a resection of a segment in three.

Damaged colon was found in 19.6% of the victims, but the damage to the intraperitoneal sections settled down. In 80% of the victims there were gut wall bruises and breaks of the serous environment. Full breaks of the wall were observed only in 20%. Half of all caecum damages settled down in the field and transverse colon. Suturing subserous hematomas and superficial breaks of the serous environment were executed in 60% of the subjects. In three cases, full breaks were observed and sutured. The wounded colon was brought forward to the abdomen wall without suturing in one. The rectum has been damaged in 3.1% wounded; its wounds were sutured in two cases and an artificial anus was placed in another.

The bladder was damaged in 2.1% of the cases, suturing was performed in one wounded, and in two victims epicyctostomy was performed. Damage of large vessels in the abdominal cavity was found in 3.1% of the victims. Broken inferior vena cava was observed in one, and porter case, veins in one and left iliac veins in one. The hematoma of mesenteries of the small intestine met in 24.7% of cases, mesenterim of colon in 15.5%, retroperitoneal hematoma in 32%, pelvic hematoma in 14.4%. Broken mesentery of the small intestine was found in 11.3% of the victims with mesenteric colon at 6.2%. The volume of the abdominal cavity contents ranged from 50 up to 4,000 ml (average volume 1,194 ± 87 ml) liquids. Blood was found in 91.8% of the cases, pus in 2.1%, intestinal contents in 10.4%, urine in 1%, and bile in 8.2% of the cases. As a rule, on a serous environment parietal peritoneum damages came to light and peritonitis was established in 14.4% of the victims.

LAND MINE INJURY MANAGEMENT

Effect of Time from Explosion to Injury Treatment

The time from acquiring an injury until the start of surgical management played an important role in reducing the mortality rate among the wounded. Table 11-4 shows how much the lag time from receiving an abdominal injury was reduced when compared to that in World War II, which contributed to reducing mortality. In a mine blast-trauma, the time elapsed from sustaining of damage before receiving any level of qualified surgical assistance was 2.7 ± 0.2 hr. (In subjects with penetrating wounds of the abdomen, the time elapsed was 3.8 ± 0.1 hr.) However, the time before surgery was initiated was longer (4.2 ± 0.1 hr), and in subjects with penetrating wounds of an abdomen, was 2.0 ± 0.1 hr.

This illustrates the greater complexity of diagnosing mine blast-trauma of the abdomen. The conditions of the victims were diagnosed as satisfactory in 4%, average in 17.3%, severe in 42.7%, and extremely severe in 36%. The number of injured complaining from spreading abdominal pain was 61.5%. Upon examination, morbidity was classified as localized in 23.9% of the victims, and spreading in 51.5%. Frequency of muscle tension of the forward abdominal wall was 62.3%, positive symptom irritation of peritoneum (Schetkin-Blumberg symptom), 55.6%. Inflated abdomen was observed in 18.6% of the victims, and peristalsis was absent

Table 11-4 Frequency of Damage to the Abdominal Organs from Penetrating Abdominal Wounds (PAW) and Mine Blast Trauma (MBT) during the Soviet–Afghan War

Organ	PAW (%)	MBT (%)
Stomach	17.6	4.1
Duodenum	4.8	1.0
Small intestines	56.4	20.6
Colon	52.7	19.6
Rectum	5.2	3.1
Liver	22.4	37.5
Spleen	6.5	54.2
Pancreas	5.7	10.3
Kidneys	11.9	11.5
Bladder	5.4	2.1
Large vessels	13.5	3.1

Table 11-5 Comparison of the Time from Receiving an Abdominal Wound until the Start of Surgical Treatment during the Soviet–Afghan War and World War II

Time (hours)	Soviet–Afghan War (%)	World War II (%)
<3	92.10	16.9
3–6	4.73	28.3
6–12	1.49	30.5
12–24	0.56	17.0
>24	1.12	6.3

in 66.7%. Practically all victims at the time of arrival to the hospital had tachycardia, and half of them had shortness of breath.

Mine victims had different levels of shock. The frequency of shock level among land mine wounded personnel is shown in Table 11-5. Basically, shock was absent in 19.3% of the wounded. Diagnosis showed shock level I in 4.5%, level II in 21.6%, level III in 21.6%, and terminal stage in 33%. Upon arrival, 51.5% of the wounded underwent radiological examination. However, this was done basically to diagnose the damaged bone structures. Laparocentesis was used in 68% of the cases, including 7% prolonged laparocentesis where blood or liquid was mixed with blood and received in 98.5% of the cases. However, in one case, despite executed laparocentesis, damage of internal organs was revealed only during operative intervention. After the sixth day at the third stage of evacuation of the victims, intraabdominal bleeding was developed. Intraabdominal bleeding was connected with a two-time break of a spleen.

First Aid

First aid was administered to 73.5% of the victims including applied aseptic bandages, 42.6%; analgesics, 64.7%; transport immobilization, 20.6%; tourniquet, 14.7% (at wounds of extremities). Infusion therapy before a staging of the qualified surgical assistance was carried out in 14.7% of the victims. The liquid volume ranged from 300 to 2,000 ml (average volume 1,006 ± 181 ml), and crystalloid solutions in 5.9% of victims, colloid solutions in 11.8%. Antibiotics were administered to one victim. Transport of the wounded was done in 53.5% of the cases by helicopters, ground transport (automobiles, armored troop-carriers) in 42.3%, and sanitary transport in 12.7. In the hospital the victims were inspected,

and catheterization and infusion therapy was carried out into peripheral and subclavian veins and proceeded as a component of preoperative preparation. This was carried out in 66.2% of the victims. The volume used ranged from 150 up to 9,600 ml (average volume 1,606 ± 188 ml). The extent of internal organ damage was not always estimated by the surgeon-on-duty, which resulted in a tightening of diagnostic process and the late beginning of operative treatment. Antibiotics were administered before operation during the preoperative preparations in 7.8% of the cases.

Operative Intervention

Operative intervention, as a rule, was carried out under endotracheal narcosis using all available medical preparations for the general multicomponent anesthesia. The volume of infusion therapy used during operations ranged from 400 to 12,100 ml (average volume 3,595 ± 260 ml). Reinfusion of blood from an abdominal cavity was done in 36.4 % of cases. The volume of reinfusion varied from 100 to 9,800 ml (average 1,788 ± 260 ml). For blockade of small intestine mesenteries 0.25% novocaine solution was used in 62.5% the cases. However, in most cases it was used before the end of operative intervention. Antibiotics during operation were administered to 18.2% of the cases. In 57% of the cases, operation began from middle-median access, and in 43% from high-median. After careful inspection of the organs in the abdominal cavity, any internal bleeding was stopped before surgical intervention of damaged organs was carried out. However, in view of the extent of internal organs damage, five wounded (5.2%) died on the operating table and 12 (12.4%) in the first day after operation.

Drainage of the small intestine by nasogastroenteral probe was carried out in 13 victims. After finishing the operation, washing of the abdominal cavity was carried out in 63.5%. The volume of a washing liquid ranged from 2 to 12l, (average 6,580 ± 390 ml). A solution of furacillinum often was used for washing, however, in a single instance a solution of chlorhexidine was used. After washing the abdominal cavity and before suturing the wound, drainage was carried out in multiple compartments. Thus, a cavity of a small pelvis was drained in 67% of the victims, omental bags in 4.1%, subliver space in 15.5%, a box of a spleen in 24.7%, subdiaphragmatic space in 10.3%, and lateral channels in 5.3%. In addition, retroperitoneal space was drained in 10.3% of the cases, paravesical space in 4.1%, and pararectal space in 2.1%.

In addition, operating on the extremities was carried out in 34% of the cases and thoracocentesis in 16.7% of the cases. It should be noted that only the time from injury to surgical treatment played a role in saving lives; the duration of operating time also played a significant role in reducing wound complication and mortality as shown in Table 11-6.

Postoperative Recovery

A smooth postoperative period was achieved in only 15.1% of the victims, and a complicated period in 84.9% of the victims. The number of postoperative complications from one wounded to anther varied from one to 15 complications. Abdominal cavity bleeding in the postoperative period was found in 4.7% of cases, arrosion bleeding in 3.6%, and gastroenteric in 2.4% of the cases. The suppuration of postoperative wounds was developed in 12.8% of the victims, a progressive peritonitis in 8.1%, intraabdominal abscesses in 5.9%, sharp intestinal obstruction in 5.9%. An inconsistency of sutured wounds of the small intestine was found in 1.2% and eventration in 1.2% of the cases. Relaparotomy concerning intraabdominal complications were executed once in 11.3% of the cases; in two cases, twice; and in one case, four times. Postbleeding anemia was found in 48.8% of cases, an ischemia of the myocardium in 43.8%, pneumonia in 22.8%, sharp renal insufficiency in 6%, and sharp hepatic insufficiency in 3.6%. Fat embolism was found in 3.6% and pleural empyema in 1.2% of the cases.

In the postoperative period infusion therapy, including blood and blood components such as rheopolyglucin, rheogluman, and Trental, was carried out. For correction of a water–salt exchange crystalloid solutions were used, including 0.9% sodium chloride solution, Ringer solution, di-salt, tri-salt, and 5% glucose solution. The balanced amino acids solutions were applied to completion of plastic resources (aminosteril, aminon, heparsteril, infusamin), power-fatty emulsions (intralipid, infusolipol),

Table 11-6 Dependence of Injury Complication and Lethality on Operation Time during the Soviet–Afghan War

Duration of Operation (hours)	All Wounded (%)	Wound Complications (%)	Dead (%)
<3 hours	52	73.2	10.3
>3 hours	48	91.8	37.6

and 20% solution of glucose. Detoxication was carried out by a method using forced diuresis (solutions hemodes, polyvisoline), and also using hemasorbtion and enterosorbtion. Peridural anesthesia for durations from one to 15 days was carried out in 30.2% of cases. Hyperbaric oxygenation was carried out in 12.8% of the cases. Intraaortic therapy was used in 6.3% of the cases. Catheterization of the umbilical vein was executed in 4.3% of the cases.

Practically all victims in the postoperative period underwent antibacterial therapy. Penicillins (benzylpenicillinum, ampicillin, oxacillin, pentrexill) were used in 68.5% of the victims, aminoglicozides (streptomycin, monomycin, canamycin, gentamycin, garamycin) in 63%, cephalosporinus (keflin, kefzol, klaforan) in 65.8%, tetracyclines (tetracyclin, morphocyclin) in 11%, lincomycin, lincocin at 5.5%, macrolides (erythromycin, oleandomycin) in 1.4%, levomycetin in 2.7%, and methronidazolum in 6.8%. Antibiotics were administered intramuscularly in 95% of the victims, intravenous in 74.6%, intraaortic in 6%, intraperitoneal in 41.8%, and endolymphatically in 3% of the cases. Peritoneal perfusion for one to five days was carried out in 6.3% of the victims.

Among the causes of death was a sharp massive loss of blood in approximately half of those who died. Peritonitis caused death in 8%, the same as pulmonary insufficiency. The medical records of casualties resulting from the land mine explosions have shown the following distribution by outcomes:

- Dead, 40.2%
- Suitable to return to war-time service, 6.4%
- Suitable for military service only in peace time (i.e., limited to suitable for first degree in wartime), 2.1%
- Suitable for nonmilitary service in war time, 32.1%
- Unsuitable for military service, 8.9%
- Short-term undetermined sickness, 10.3%

The average duration of mine victims' treatment was 75.5 ± 13.6 days. Thus, explosive damages of organs of the abdominal cavity, especially mine-blast trauma, cause combined damages with a high level of lethality and pension off victims. Such wounded demand the most steadfast attention at triage, operative, and postoperative treatment at all stages of medical evacuation.

CONCLUSIONS

In conclusion, the most important lesson learned from the Afghan war is that blast injuries to organs of the abdominal cavity, particularly mine-blast trauma, are severe and complex injuries with high potential for complication and mortality. Victims of blast injuries require continuous attention from the time they are injured until they are evacuated, and at all stages of treatment including preoperative, during operation, and post-operative care. The Soviet military experience showed that what killed the wounded was not the loss of a limb to mine blast, but rather shock and the combination of injuries to internal organs after bleeding was successfully stopped. It was learned that normal treatment time periods may not apply and, although emergency surgery often was necessary, it was better to be sure that the patient was stabilized before starting any surgery. It was also discovered that performing multiple surgical procedures at the same time, though increasingly common under ideal circumstances, was not a good idea and that it should be done only to save the patient's life. Finally, it was found that with land-mine injuries, surgical procedures should be performed sequentially, rather than simultaneously.

DISCLAIMER

The views and opinions expressed herein are the private views of the author and are not to be construed as official nor do they reflect the views of the Ministry of Defense.

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CHAPTER 12

Otologic Blast Trauma: Experience from Croatian War

Srećko Branica, Krsto Dawidowsky, Nikola Šprem, and Brian McKinnon

"The task of medicine: Cure sometimes; relieve often; care always."
Ambrose Pare, father of modern surgery 1510–1590

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INTRODUCTION

Following independence in the autumn of 1991, The Republic of Croatia was almost immediately under siege by the forces of the former Yugoslav People's Army, and Serbian paramilitary forces composed of ethnic Serbians living in Croatia. The republic was unprepared for armed conflict, having no military resources of its own, whereas the republic's opponents were well organized, having use of the assets of the former Yugoslav People's Army. During this profoundly violent and brutal confrontation, Croatians organized their defense forces, including a military health system.

Early in the war, Croatia lacked qualified military personnel, medical and transportation equipment, medications and other medical provisions.

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Care for military casualties was managed within the civilian health system, under the supervision of the Ministry of Health. Headquarters of the Medical Corps was established by the Ministry of Health as the responsible institution for the organization of wartime health care. Civilian hospitals near the battlefield were transformed for the purpose of accepting combat casualties. Those hospitals closest to the frontline with large numbers of well-trained civilian medical personnel underwent urgent military medical and surgical education. Simultaneously, the founding of official military medical units provided for medical support to be integrated into army units. From the beginning, the military and civil health systems were organized as a single, collaborative, integrated health system (Hebrang 1992; Hebrang et al. 2006). As previous modern European conflicts had occurred between armed forces with well-organized military medical commands operating separately from civilian medical systems, this integrated civilian-military system is unique.

As experience with integrated civilian-military medical systems was unusual in Europe (Rozin 1986), organization of Croatian war medical system was influenced and modeled by the Republic's needs and circumstances (Hebrang 1992; Hebrang et al. 2006). First aid and initial stabilization of the wounded on the frontline and the transport of casualties were part of the military organization. Definitive tertiary medical care took place in civilian hospitals converted to military use, typically near the frontline, with necessary additional medical personnel and equipment detached as needed. An important element was mobile teams of physicians positioned closer to the frontline than in previous European wars. Improvised hospitals were established in forward areas when the distance between the frontline and established hospitals was too great. Patients who needed additional or specialized medical care were transported to other civilian hospitals for those treatments.

Analysis of military and civilian casualties care published 10 years after the war demonstrated impressive results in overall patient survival (Hebrang et al. 2006). Data available from all Croatian military and civilian hospitals on 30,520 of the 43,476 war casualties treated during the war indicates 23.5% of the casualties were civilians. This was a grim result of the former Yugoslav army's and Serbian paramilitary's strategy of surrounding towns and shelling civilian targets for months. Following injury, 61.1% of the wounded were transported to the nearest hospital within one hour of injury, and 76.3% of the wounded within two hours of injury. A total of

42,239 inpatient operations were performed, with recovery and improvement in 81% of all treated cases. Overall mortality rate of the wounded was 1.49%, inclusive of the 15,000 wounded patients treated as outpatients.

An important aspect of the Croatian combat health care organization was the cooperation between the first responder and transport teams organized by military medical teams, and the civilian hospitals modified for the reception of wounded military personnel, resulting in patients receiving very good definitive treatment. The integrated civilian-military medical service in collaboration with excellent medical staff of the civilian hospitals during the Croatian conflict resulted in successful hospital treatment and a very low mortality rate in the combat injured.

WAR-RELATED BLAST INJURY OF THE MIDDLE EAR

Explosions (blasts) produce an air pressure wave that traumatizes the human body in various ways. The ear is a highly susceptible organ to the action of the air pressure wave, with tympanic membrane and inner ear trauma common. On explosion, an instantaneous positive wave of air pressure is produced. This positive wave can disrupt or perforate the tympanic membrane, and less frequently, dislocate or interrupt the ossicular chain, rupture the round window, or displace the stapes footplate. The positive wave of air pressure is followed by a prolonged but less intensive negative wave, as predicted by Friedlander's curve. This negative wave affects the ear to a considerably lesser extent (Pahor 1981; Sudderth 1974; Šprem & Branica 1992). The power of the positive wave depends on the strength of the explosion and on the distance from the site of the explosion the individual is. Trauma is more severe if the explosion occurs indoors because the positive pressure wave reflects from the walls. Tympanic membrane perforation may occur at a pressure of not more than 35 kPa, and a pressure of 105 kPa causes perforation in 50% of adult tympanic membranes. A pressure required for lesions of the lungs and gastrointestinal system to occur is considerably higher, thus those wounded by blast and found to have the respiratory or gastrointestinal trauma would be expected to have tympanic membrane trauma as well.

About 80% of all blast induced tympanic membrane perforations heal spontaneously, 40 to 50% of them within the first month, and more than 60% within the first two months. Spontaneous healing is influenced by the size

and localization of the defect. However, if spontaneous healing does not begin within the first month, the epithelium on the lateral surface of the tympanic membrane will overgrow the rim of the defect and spontaneous healing is very unlikely to occur. With blast, tympanic membrane remnants can be planted in the middle ear and the defect's rim may fold medially. After spontaneous healing, cholesteatoma may form at these sites (Pahor 1981; Kerr & Byrne 1975; Roth et al. 1989; Singh & Ahluwalia 1968).

Surgical techniques used in the treatment of tympanic membrane blast trauma include tympanic membrane remnant repositioning with insertion of silicone foil, paper, or Gelfilm over the tympanic membrane; tympanoplasty and myringoplasty using any number of different materials including perichondrium, temporalis fascia, or heterograft; and, quite infrequently, electrocoagulation of the defect rim to stimulate spontaneous healing (Šprem et al. 1992; Messervy 1972; Ruggles & Votypka 1973; Makki 1989).

Spontaneous Healing and Repositioning

The ear canal and tympanic membrane can be debrided, and the torn and folded parts of the tympanic membrane repositioned several days after a blast injury. Pieces of resorptive gelatin are placed into the middle ear space to position the folded and torn parts of the tympanic membrane, and the perforation is covered with silicone foil, paper, or Gelfilm. Using this technique, with silicone foil left on the ear-drum for four weeks, spontaneous healing of the tympanic membrane is stimulated; the possibility of cholesteatoma is reduced by removing the tympanic membrane debris from the middle ear space and repositioning of the remaining tympanic membrane remnant (Messervy 1972).

Minor tympanic membrane defects were left to heal spontaneously. As these were small perforations, their mean conduction hearing loss on admission was lower than the more extensive otologic trauma that was surgically managed. After spontaneous healing, the hearing loss subsided almost completely, resulting in a mean 4 dB air-bone gap. Tympanic membrane repositioning with the placement of silicone foil was performed within a short time of injury in the wounded admitted to our department during the war. This procedure was used in patients with defects less than 50% of the tympanic membrane. The mean postoperative conduction hearing loss after the removal of the silicone foil (four weeks after the procedure) was 6 dB air bone gap.

Although the mean hearing recovery after tympanic membrane repositioning and silicone foil placement over the tympanic membrane was 10 dB, results differed in relation to the time period elapsed between the wounding and repositioning. A negative correlation coefficient indicated that a delay in treatment for these injuries decreased the level of hearing recovered. Those in whom repositioning was performed in 48 hours from the injury, hearing recovery ranged between 10 and 20 dB, with a mean of 13 dB; if repositioning was performed after more than a week post-injury, the recovery of hearing was half as much (see Figure 12-1). This was due to the epithelium, during the first few weeks, gradually growing over the lateral side of the tympanic membrane and traumatic rim, preventing spontaneous healing.

In some wounded patients, especially those with major and multiple traumatic injuries, otoscopic exam was delayed more than a month after the injury. In the most severe cases, who would have been managed by repositioning if diagnosed earlier, we performed tympanoplasty. When possible, we strongly recommend all wounded by blast should undergo early otologic exam.

Tympanoplasty

Some authors advocate tympanoplasty and myringoplasty immediately after injury (Ruggles & Votypka 1973), arguing that the possibility for the infection of the exposed middle ear is reduced. Other authors suggest the blast lesions of tympanic membrane be left to heal spontaneously, and only perforations that do not heal within several months, or total tympanic membrane perforations (where spontaneous healing would not be expected) should be surgically managed (Kerr & Byrne 1975).

In tympanic membrane trauma that was not hospitalized immediately after injury, or in cases of total and subtotal perforation, tympanoplasty or myringoplasty was performed. As total perforations, the mean preoperative hearing loss was higher than in those who were eligible for treatment with the placement of silicone foil (about 19 dB). The mean postoperative hearing loss was also higher than in those managed with the placement of silicone foil (about 10 dB).

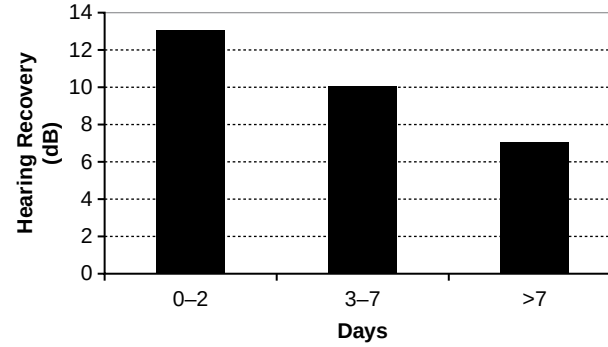

FIGURE 12-1
Mean value in the recovery of hearing in dB after eardrum repositioning and placement of silicone foil relative to the number of days elapsed between the wounding and the foil placement.

We tested different materials to determine which one is the most suitable for tympanic membrane repair after blast injury. In addition, in order to maximally preserve hearing, we wanted to determine the best time to perform tympanoplasty following blast injury. The number of ear blast injuries during the 1991–1995 war in Croatia enabled us to evaluate with a large sample whether the time elapsed between injury and tympanoplasty influenced the success rate of tympanoplasty.

From the beginning of the war in Croatia in 1991 until the end of 2000, we treated 651 patients for blast injury of the ear, out of whom 403 had bilateral ear injury. Out of the total of 1,054 ear blast injuries, 444 (42%) were injuries with mixed hearing loss, 493 (47%) with pure sensorineural hearing loss, and 117 (11%) with pure conductive hearing loss without internal ear damage. Patients who had had preexisting ear problems (chronic otitis, hypoacusis, or previous ear surgery) before the blast injury were not included with those having the blast injury alone. Of the total of 561 cases with conductive hearing loss (444 mixed hearing loss and 117 pure conductive hearing loss), 549 were tympanic membrane perforations, 9 were tympanic membrane perforations with dislocation or interruption of the chain of auditory ossicles, and 3 were hematotympanum.

Tympanoplasty was performed in 172 out of 549 cases with tympanic membrane perforations without dislocation or interruption of the ossicles chain, and was not performed in cases of small tympanic membrane defects (up to 50% of tympanic membrane), because spontaneous healing was expected. Our study included a total of 161 tympanic membrane perforations (106 patients) with 11 cases excluded from the study since patients were lost to follow-up. Tympanoplasty was performed unilaterally in 51 and bilaterally in 55 of them. Inclusion criteria were injuries with tympanic membrane perforation, patients with regular postoperative clinical and audiological follow-up, and patients with follow-up time longer than two years. Exclusion criteria were injuries with dislocation or interruption of the chain of auditory ossicles and injuries with hematotympanum. There were 105 men and 1 woman, aged 18 to 54 years (mean 28.1 ± 7.2 years). The right ear was injured in 82 (51%) cases and the left ear in 79 (49%) cases. All patients received 500-mg amoxicillin three times a day, for five days, as postoperative antibiotic prophylaxis. Suppuration after injury was observed in 21 (13%) out of 161 injuries. After the cessation of suppuration, at least one month had been

allowed to elapse before the surgery was performed in these patients. To close the tympanic perforation we used temporalis fascia in 81 cases (50%), tragal perichondrium in 61 cases (38%), and heterograft (absorbable durra mater substitution from bovine collagen) in 19 cases (12%). Median number of days between the injury and tympanoplasty was 79 (range, 4 days to 5 years, 7 months, and 12 days). According to the number of days elapsed between the injury and the surgery, we divided all injuries into four groups: 0–20 days, 21–60 days (when spontaneous healing is finished in most injuries), 61–180 days (spontaneous healing must be finished in all injuries), and 181 days and more (Wolf et al. 1991; Messervy 1972).

Otomicroscopy and audiometry were performed 2, 6, 12, and 24 months after the surgery. We used the last audiometry result as the definitive result. Tympanometry was performed in all patients to confirm the closure of tympanic membrane defect. In the blast lesion of the tympanic membrane, conduction hearing loss was not always present in all the frequencies. Low frequencies of less than 1,000 Hz were affected in 80% to 86%, and frequencies of 2,000 to 6,000 Hz in 97 to 99% of the cases. The high frequency hearing loss was more severe than the low frequency hearing loss.

Tympanoplasty Results by the Material Used

In contrast to other authors (Wolf et al. 1991; Kerr & Byrne 1975; Pahor 1981; Sudderth 1974; Berger et al. 1994; Singh & Ahluwalia 1968), who used only temporalis fascia and perichondrium from the tragus for the tympanic membrane repair, we also have used a heterograft, with the same success rate. For all three materials used, the success rate was 89 to 92%. The results showed no difference in success in the tympanic membrane perforation closure rate or in the postoperative air-bone gap among the three patient groups when analyzed according to the materials used. All three materials—temporalis fascia, tragal perichondrium, and heterograft—can be used successfully for the tympanic membrane perforation closure after blast injury (Šprem et al. 2001a).

In conclusion, tympanoplasty using any of the three materials (temporal fascia, perichondrium, or heterograft) for blast-induced tympanic membrane perforation was successful in 89 to 92% of tympanic membranes. There was no significant difference in the values of postoperative air-bone

Table 12-1 Success Rate of Tympanoplasty and Postoperative Air-Bone Gap (mean ± SD) According to the Material Used for Reparation of the Injured Eardrums (n = 161)

Grafting Material	Success Rate	Postoperative Air-Bone Gap (dB)[a]
Fascia	74/81 (91%)	5.3 ± 4.9
Perichondrium	56/61 (92%)	5.5 ± 4.3
Heterograft	17/19 (89%)	6.7 ± 7.3

[a]*Kruskal-Wallis test = 1.694; p = 0.429.*

gap (conductive component of hearing loss) among the patient groups analyzed according to the used material (see Table 12-1).

Tympanoplasty Success Rate According to the Time Elapsed between Injury and Tympanoplasty

When comparing the success of the tympanoplasty performed at different times following blast injury, we found no significant difference among the groups (see Figure 12-2). The rate of successful tympanic membrane repair was between 89.3 and 93.0% in all four groups of injuries, with no significant difference in postoperative air-bone gap (see Table 12-2). Comparison of the postoperative air-bone gap with the number of days elapsed between the wound infliction and tympanoplasty showed no correlation either.

Also, there was no correlation between the time passed from the injury to the tympanoplasty and the success of the operation measured by the air-bone gap in the postoperative audiogram. Since the probability of spontaneous healing of the large defects of the tympanic membrane is very low, the

Table 12-2 Success Rate of Tympanoplasty and Postoperative Air-Bone Gap (mean ± SD) According to the Number of Days between the Injury and the Tympanoplasty (n = 161)

No. of Days between Injury and Tympanoplasty	Success Rate	Postoperative Air-Bone Gap (dB)[a]
0–20	25/28 (89%)	6.4 ± 4.2
21–60	38/42 (90%)	5.3 ± 5.5
61–180	40/43 (93%)	4.9 ± 2.4
>180	44/48 (92%)	5.9 ± 6.6

[a]*Kruskal-Wallis test = 4.523, p = 0.210.*

postponement of the tympanoplasty increases the possibility of ear inflammation (Ruggles & Votypka 1973). Therefore, tympanoplasty should be performed without delay on all total and subtotal tympanic membrane perforations.

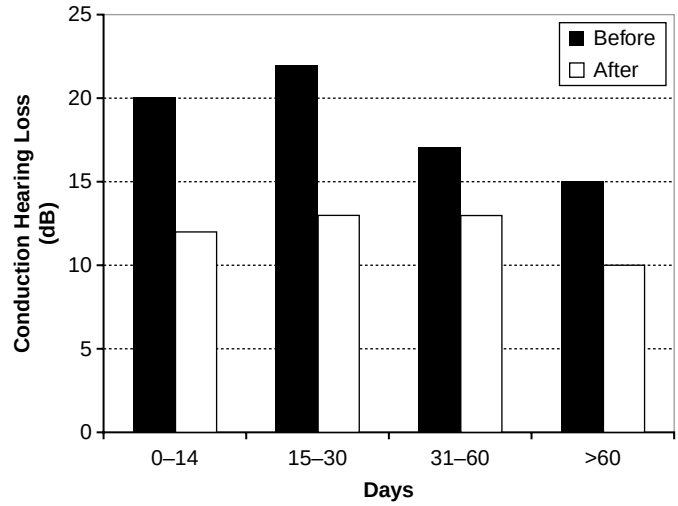

FIGURE 12-2
Mean value in conduction hearing loss before and after tympanoplasty relative to the number of days elapsed between the wounding and the surgery.

It seems the success of the tympanoplasty remains the same, even if the surgery is performed six months or more after the blast injury. This finding implies that we can wait for the spontaneous healing for a long period of time, except in the cases of total and subtotal perforations and spontaneous healing failure. Air blast may induce tympanic membrane perforation, internal ear lesion, or both. In our study, conductive hearing loss was almost exclusively caused by the tympanic membrane perforation (97.9%). The chain of auditory ossicles was interrupted in nine cases (1.6%), which was less than in another study (Sudderth 1974). We have also had three cases of hematotympanum, which other authors usually do not describe (Wolf et al. 1991; Šprem et al. 1992).

The conductive hearing loss caused by the blast injury of the tympanic membrane involves high frequencies more frequently, usually those between 2 and 6 kHz. Unlike the conductive hearing loss due to the tympanic membrane perforation in chronic otitis, the conductive hearing loss due to the blast injury more severely affects high frequencies than the low ones, up to 11 dB on average.

Even with the large number of patients, this study would have greater weight had it been prospective and the patients randomized to various treatment options. Practically, it could not have been done. In 1991 all hospitals worked under the unfavorable conditions of war (Lackovic et al. 1992) and had to take care of many wounded rapidly, effectively, and efficiently. For example, the reason why a particular material for tympanoplasty was used depended mainly on the free choice of the surgeon in each particular case.

The small differences in the recovery of hearing and the extent of postoperative hearing loss following tympanoplasty gives the appearance that success

of tympanoplasty to be independent of the time elapsed between the injury and repair. However, in those wounded in which tympanoplasty was performed more than two months after injury, the postoperative conduction hearing loss averaged about 2 dB greater than those operated on less than two months after injury. This is reflected in a lower preoperative conduction hearing loss in the wounded operated on later (Šprem et al. 2001a).

We are inclined to recommend all fresh blast induced tympanic membrane perforations (except the total and subtotal perforations), especially those hospitalized within 48 hours, undergo repositioning of the tympanic membrane remnant and covered with silicone foil or Gelfilm. The advantage of this procedure on the ear is its simplicity, and is conducive to being performed simultaneously with the surgical management of other blast injuries. In all blast-induced tympanic membrane perforations that do not heal spontaneously and in subtotal and total tympanic membrane perforations, myringoplasty or tympanoplasty should be performed.

WAR-RELATED BLAST INJURY OF THE INNER EAR

Conductive hearing loss develops after damage to the tympanic membrane, disruption of the ossicular chain, or hematotympanum (Perez 2007; Berger et al. 1994; Aktas & Kutlu 2000; Šprem & Branica 1992), whereas sensorineural hearing loss results from damage to the internal ear (Garth 1994; Cudennec et al. 1995). In some patients, sensorineural hearing loss caused by blast injury may recover during the first few weeks, although usually only partially. After that time, permanent hearing loss cannot be cured by current methods or surgically recovered like conductive hearing loss.

Therapy for sensorineural hearing loss is controversial. Some studies have demonstrated the effectiveness of various drugs including vasodilators, anticoagulants, and steroids on recovery of hearing (Moskowitz et al. 1984; Wilson et al. 1980; Kubo et al. 1988), whereas others have shown no effect of these interventions on sensorineural hearing loss (Byl 1984; Kronenberg et al. 1992; Kanzaki et al. 1988). Evaluation of a medication's effectiveness on the treatment of sensorineural hearing loss is difficult due to the incidence of spontaneous hearing recovery (Anderson & Meyerhoff 1983; Mattox & Simmons 1977; Simons 1977). The therapy of blast injury sensorineural hearing loss caused by war is even less researched.

From the beginning of the War in Croatia in 1991 until the end of year 2000 in the ENT Department Šalata, 558 patients were treated from the inner ear blast injury—551 (99%) men and seven (1%) women. Among them, 385 wounded patients suffered bilateral injury, so that a total of 943 inner ear blast injuries were treated. Out of 943 injuries, 469 (50%) were injuries of the left ear, and 474 (50%) were of the right ear.

Our hospital was located close to the front line, and a majority of the injured were examined and treated shortly after the blast trauma. The patients were evaluated and audiometry performed immediately after the admittance to the ENT department. The period between injury and initial audiometry ranged from several hours to two years and eight months after the blast injury, though the median was two days. Of the 555 internal ear injuries examined, 384 were within the first two days after the injury.

As in other studies (Perez et al. 2000), the frequencies of 3 kHz, 4 kHz, 6 kHz, and 8 kHz were most frequently affected and were more severely damaged than lower frequencies by the blast. The average sensorineural hearing loss in patients measured within the first two days following the blast injury was 26.4 dB.

At the beginning of the war in Croatia, some of the patients with blast-induced sensorineural hearing loss were treated with vasodilators (Šprem et al. 2001b). There were 82 patients (119 injuries) in the group that received vasodilator treatment that consisted of 250 ml saline infusion with vasodilator pentoxifylline 100 mg and the following vitamins: thiamin (B1 vitamin) 250 mg, pyridoxine-chloride (B6 vitamin) 250 mg, and ascorbic acid (C vitamin) 1.000 mg. The therapy was introduced within the first two days from the blast injury and continued for 10 days.

Since the success of vasodilators in recovering hearing was dissatisfying, we decided to treat blast-induced sensorineural hearing loss with steroids. A total of 166 ear injuries (i.e., 98 patients) were treated with methylprednisolone or prednisolone as therapy. First-day therapy dosage varied between 32 mg and 64 mg, and during two to three weeks was gradually reduced to 4 mg.

Some patients (149 injuries of the inner ear or 87 patients) did not receive any therapy because of medical contraindications, other more urgent injuries, combat demands, and other reasons.

Hearing recovery was evaluated using the average hearing level in the initial stage, four to five days, eight to ten days, a month, three months, six months, and a year after the beginning of treatment. The last audiometry (after one year) was considered definitive.

Six months and more after the therapy, when the function of the inner ear after blast injury and treatment had stabilized, the average value of the sensorineural hearing loss in the group of patients who received vasodilator and vitamins therapy improved by 7.0 dB compared to the value before the therapy. In the group of patients who received no therapy average value of sensorineural hearing loss six months and more from the blast injury was 6.8 dB better than immediately after blast injury. The difference between the groups, however, was not statistically significant.

Of the 166 patients with the internal ear injuries administered the steroid therapy, the average sensorineural hearing loss six or more months after the therapy, the time at which post injury inner function had stabilized, was 11.3 dB better than before the therapy. This improvement was statistically significant compared to the group of patients who received no therapy or who received vasodilators and vitamins.

Sensorineural hearing loss after blast injury is caused by inner ear damage (Wilson et al. 1980; Kubo et al. 1988). In the process of recovery of sensorineural hearing loss, circulation and oxygen availability could play a role. Lamm (1988) showed that oxygen partial pressure in scala tympani was lower after blast injury. Experimental data on the pharmacology of the inner ear showed that better circulation could induce better recovery of sensorineural hearing loss after acoustic trauma induced sudden deafness. Other authors assert that better recovery could be achieved if infusion with vitamins and vasodilators or therapy with hyperbaric oxygenation was administered immediately after the blast injury. Steroids may have a similar positive effect on the blast traumatized inner ear as they can reduce edema and improve microcirculation.

In spite of the fact that infusion therapy with vasodilators and vitamins therapy was started within the first two days from the blast injury or immediately after the initial audiological testing, we did not find any evidence that infusion therapy with vasodilators and vitamins had a positive influence on blast-induced sensorineural hearing loss recovery. This was in concordance with findings in some previous studies performed on a similar number or smaller number of patients (Garth 1994). Although inner ear recovery

after steroids therapy was not complete, it was significantly better compared to no therapy or therapy with vasodilators and vitamins.

The review's limitation is as a retrospective study. More convincing results could have been produced by a prospective randomized placebo-controlled study on the same number of patients. However a prospective randomized placebo-controlled study was not possible under the conditions of a war and a high number of wounded. Therefore we could not achieve proper randomization or placebo control. Patient allocation to either control or treatment group was biased to the supposed beneficial effect of treatment with vasodilators, vitamins, and steroids than to no effect. The control, or no treatment, group was composed of patients that were in a more serious medical condition or had other injuries that needed further and urgent treatment, whereas the treatment group stayed within our department for ongoing care.

We diagnosed more pure sensorineural and less conduction hearing losses than some other authors (Berger et al. 1997; Walsh et al. 1995). This can be explained by the timing of audiometry tests in our patients, which was completed within the first two days following injury. In this way we have managed to avoid patients with spontaneous healing of sensorineural blast injury that is very intensive during the first few days after injury infliction.

Our experience on a large number of patients, despite limitations, showed that war-related blast injuries to the internal ear follows its natural course of healing regardless of the adjuvant therapy with vasodilators and vitamins. Steroids showed a statistically significant positive influence on inner ear healing after blast injury.

SUMMARY

To respond to the armed conflict that occurred with the Republic of Croatia's declaration of independence, the Republic had to rapidly organize its nation's defense. This included the partnering of civilian and military health care in a manner that previously had not been seen in past European conflicts. The result was a successful, effective, and efficient civilian-military health system that provided high quality care for the over 43,000 military and civilian wounded during the war.

Blast is a trauma common to modern war, and is uniquely injurious to the ear. Ear trauma should be expected and looked for in those suffering from

blast injuries, particularly those who suffer from blast-related pulmonary and gastrointestinal injuries. Tympanic membrane trauma should be addressed as early as possible, with perforations less than 50% of the tympanic membrane treated with debridement, and repositioning of the remnant. Those tympanic membrane defects that do not spontaneously heal despite treatment or because of size can be surgically repaired using a variety of materials successfully. Those with blast-induced sensorineural hearing loss may benefit from the use of steroids.

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